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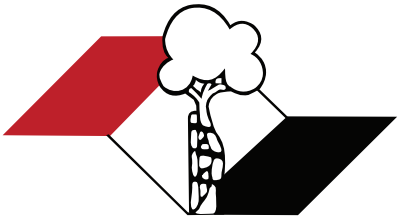

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CHEGOU

FOXIS
CELECOXIBE

Eficácia, segurança e preço acessível no tratamento anti-inflamatório.[1-4]

- **Melhora significante** dos sinais e sintomas de osteoartrite.[6]
- **Eficaz** no tratamento de dor aguda.*[7]
- Inibidor da COX-2 **mais utilizado no mundo.**[5]

* Devido a entorse de tornozelo em 24 horas após o início do tratamento.

Referências bibliográficas: 1. SIMON, L.S. et al. Anti-inflammatory and upper gastrointestinal effects of celecoxib in rheumatoid arthritis: A randomized controlled trial. JAMA, v. 282, n. 20, 1999. **2.** ESSEX, M.N; BHADRA, P; SANDS, G.H. Efficacy and tolerability of celecoxib versus naproxen in patients with osteoarthritis of the knee: a randomized, double-blind, double-dummy trial. The journal of international medical research, v. 40, p. 1357-1370, 2012. **3.** LÉRIAS, J.R. Celecoxibe e rofecoxibe: eficácia e segurança dos inibidores selectivos da Cox-2 comparativamente aos AINEs não selectivos. Rev Port Clin Geral, v. 20, p. 47-64, 2004. **4.** Kairos Web Brasil. Disponível em: <http://brasil.kairosweb.com>. Acesso em: Fev. 2017.**5.** SOLOMON, S.D. et al. Cardiovascular risk of celecoxib in 6 randomized placebo-controlled trials: The cross trial safety analysis. Circulation, v. 117, p. 2104-2113, 2008.2008. **6.** BENSEN, W.G. et al. Treatment of osteoarthritis with celecoxib, a cyclooxygenase-2 inhibitor: A randomized controlled trial. Mayo ClinProc, v. 74, p. 1095-1105, 1999. **7.** CARDENAS-ESTRADA, E. et al. Efficacy and Safety of Celecoxib in the Treatment of Acute Pain due to Ankle Sprain in a Latin American and Middle Eastern Population. The Journal of International MedicalResearch, v. 37, p. 1937-1951, 2009. **8.** Internal report. **9.** Bula do produto FOXIS: cápsulas. Farmacêutica Responsável: Gabriela Mallmann. Guarulhos, SP. Aché Laboratórios Farmacêuticos S.A.

FOXIS - celecoxibe. Cápsulas. 200 mg. USO ORAL. USO ADULTO. Indicações: Tratamento dos sinais e sintomas da osteoartrite e da artrite reumatoide; alívio dos sinais e sintomas da espondilite anquilosante; alívio da dor aguda (principalmente no pós-operatório de cirurgia ortopédica ou dental e em afecções musculoesqueléticas), alívio dos sintomas da dismenorreia primária e da lombalgia. **Contraindicações:** Não deve ser usado por pacientes: que tenham tido crise de asma, urticária ou reações alérgicas após uso de ácido acetilsalicílico ou outros anti-inflamatórios; com doença hepática e/ou com insuficiência renal grave; que tenham dor relacionada à cirurgia de revascularização do miocárdio; com hipersensibilidade ao celecoxibe ou a qualquer componente da fórmula. **Cuidados e advertências:** O uso de AINEs pode retardar ou inibir a ovulação, o que pode estar associado com a infertilidade reversível em algumas mulheres. Não deve ser usado por grávidas sem orientação e seguimento médico; especialmente durante o primeiro e segundo trimestres. O uso de celecoxibe durante a gravidez requer que se pesem os potenciais benefícios para a mãe e riscos para a criança. **Celecoxibe é um medicamento classificado na categoria C de risco de gravidez.** Embora reduza o risco de desenvolvimento de complicações gastrintestinais associadas ao uso de anti-inflamatórios, esse risco não está eliminado pelo uso de celecoxibe, sendo maior em maiores de 65 anos, consumo de bebidas alcoólicas ou com história anterior de perfuração, úlcera ou sangramento gastrintestinal. Celecoxibe deve ser usado com cautela em pacientes com: hipertensão, pois pode piorá-la; portadores de insuficiência renal, alterações da função hepática em idosos; portadores das alterações das enzimas metabolizadoras CYP2C9. Celecoxibe deve ser descontinuado ao aparecimento de rash cutâneo, lesões nas mucosas ou outros sinais de alergias.**Interação medicamentosa:** anticoagulantes; anti-hipertensivos das classes dos inibidores da enzima conversora de angiotensina (ECA) e/ou antagonistas da angiotensina II diuréticos e betabloqueadores podem ter seu efeito reduzido; em pacientes idosos, com desidratação (incluindo aqueles em tratamento com diuréticos) ou com função renal comprometida, a coadministração de antiinflamatórios, incluindo os inibidores específicos da COX-2, com inibidores da ECA, pode resultar no comprometimento da função renal, incluindo possível insuficiência renal aguda; fluconazol pode aumentar os níveis sanguíneos de celecoxibe; lítio pode ter seu nível sanguíneo aumentado; medicamentos anti-inflamatórios podem aumentar o risco de toxicidade no rim associada à ciclosporina; a administração concomitante de dextrometorfano ou metoprolol com celecoxibe 200 mg duas vezes ao dia resultou em aumento de 2,6 vezes e 1,5 vezes das concentrações no sangue de dextrometorfano e metoprolol, respectivamente; fisinopril administrado concomitante com celecoxibe pode não controlar a pressão alta. **Foxis 200 mg: Este produto contém o corante amarelo de TARTRAZINA que pode causar reações de natureza alérgica, entre as quais asma brônquica, especialmente em pessoas alérgicas ao ácido acetilsalicílico. Atenção: Este medicamento contém Açúcar, portanto, deve ser usado com cautela em portadores de Diabetes. Reações adversas: Comuns** (ocorre entre 1% e 10% dos pacientes) inflamação dos brônquios e seios da face, infecção do trato respiratório superior, infecção urinária, insônia, tontura, hipertensão e piora da hipertensão, tosse, vômito, dor abdominal, dispepsia, flatulência, prurido, rash, edema periférico. Incomuns (ocorre entre 0,1% e 1% dos pacientes): faringite; rinite, anemia, hipersensibilidade, ansiedade, hipertonia, sonolência, visão borrada, zumbido; palpitação, úlceras no estômago; doenças dentárias; aumento da quantidade de enzimas hepáticas, urticária, equimose, edema facial, doença semelhante à gripe, lesão. Infecção pela bactéria Heliocobacter, pelo vírus Herpes zoster, infecções na pele, em feridas e gengiva, labirintite, infecção por bactéria, lipoma, distúrtio do sono, infarto cerebral, hemorragia conjuntival, depósitos no humor vítreo, hipoacusia, angina instável, insuficiência da valva aórtica; aterosclerose da artéria coronária; bradicardia sinusal, hipertrofia ventricular; trombose venosa profunda; hematoma; disfonia, sangramento da hemorroida; evacuações frequentes; ulceração da boca; estomatite; dermatite alérgica; cisto sinovial, noctúria, cisto ovariano, sintomas da menopausa; sensibilidade nas mamas; dismenorreia; aumento da quantidade de potássio e sódio no sangue, redução da testosterona no sangue; redução do hematócrito, aumento nos níveis de hemoglobina, fraturas, epicondilite, ruptura do tendão. Posologia: Celecoxibe deve ser engolido com ou sem alimentos. Para o tratamento de dor aguda e dismenorreia primária: 400 mg na primeira dose, seguidos de uma dose de 200 mg por via oral após 12 horas, seguido de 200 mg a cada 12 horas nos dias seguintes conforme necessário. Uso para o tratamento de dor crônica: menor dose diária eficaz durante o menor período possível. As doses sugeridas de celecoxibe para essas doenças são as seguintes: Osteoartrite e Espondilite anquilosante: 200 mg em dose única ou 100 mg duas vezes; Artrite reumatóide: 100 ou 200 mg duas vezes ao dia; Lombalgia: 200 mg ou 400 mg em dose única ou dividida em duas vezes de 100 mg ou 200 mg. SE PERSISTIREM OS SINTOMAS, O MÉDICO DEVERÁ SER CONSULTADO. **VENDA SOB PRESCRIÇÃO MÉDICA. SÓ PODE SER VENDIDO COM RETENÇÃO DA RECEITA. MS - 1.0573.0491. MB 02 VP_SAP 4591400_SAP 4585100. *Material técnico científico de distribuição exclusiva a profissionais de saúde habilitados à prescrição e/ou dispensação de medicamentos.**

CONTRAINDICAÇÕES: Não deve ser usado por pacientes: que tenham tido crise de asma, urticária ou reações alérgicas após uso de ácido acetilsalicílico ou outros anti-inflamatórios; com doença hepática e/ou com insuficiência renal grave; que tenham dor relacionada à cirurgia de revascularização do miocárdio; com hipersensibilidade ao celecoxibe ou a qualquer componente da fórmula. **INTERAÇÕES MEDICAMENTOSAS:** Anticoagulantes; anti-hipertensivos das classes dos inibidores da enzima conversora de angiotensina (ECA) e/ou antagonistas da angiotensina II diuréticos e betabloqueadores podem ter seu efeito reduzido; em pacientes idosos,) ou com função renal comprometida, a coadministração de anti-inflamatórios, incluindo os inibidores específicos da COX-2, com inibidores da ECA, pode resultar no comprometimento da função renal, incluindo possível insuficiência renal aguda; fluconazol pode aumentar os níveis sanguíneos de celecoxibe; medicamentos anti-inflamatórios podem aumentar o risco de toxicidade no rim associada à ciclosporina.

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ACTA ORTOPÉDICA BRASILEIRA

INSTRUCTIONS TO AUTHORS

(Reviewed January 2016)

The journal *Acta Ortopédica Brasileira*, official organ of the Department of Orthopedics and Traumatology, Faculdade de Medicina da Universidade de São Paulo (DOT/FMUSP), is published bimonthly in six issues per year (Jan/Feb, Mar/Apr, May/Jun, Jul/ Aug, Sep/Oct, and Nov/Dec) with Portuguese and English printed and online versions. *Acta* is distributed to orthopedists and leading educational and research institutions in Brazil. The publication follows entirely the international standard of the International Committee of Medical Journal Editors (ICMJE) - Vancouver Convention - and its uniform requirements [http://www.icmje.org/]. Submitted papers are sent for double-blind peer review evaluation to decide whether they should be published or not, suggesting improvements, asking the authors for clarification and making recommendations to the Editor-in Chief. The concepts and statements contained in the papers are the sole responsibility of the authors.

We ask authors to observe the following instructions for publication.

ARTICLES FORMAT

NUMBER OF WORDS RECOMMENDED ACCORDING TO THE PUBLICATION TYPE: The criteria specified below should be observed for each type of publication. The electronic counting of words should start at the Introduction and end at the Conclusion.

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Type of Article	Abstract	Number of words	References	Figures	Tables	Maximum number of authors allowed
Original	Structured, up to 200 words	2.500 Excluding abstract, references, tables and figures	20	10	6	6
Update / Review*	Non-structured, up to 200 words	4.000 Excluding abstract, references, tables and figures	60	3	2	2
Editorial*	No abstract	500	0	0	0	1

*These contributions shall be published at the Editors' criteria, with due replica, when applicable.

MANUSCRIPT PREPARATION: The journal *Acta Ortopédica Brasileira* receives the following types of contributions: Original Article, Update Article and Review Article. The Update and Review articles are only considered by invitation from the Editorial Board.

Manuscripts should be sent in .txt or .doc files, double-spaced, with wide margins. Measures should be expressed in the International System (*Système International*, SI), available at http://physics.nist.gov/cuu/Units and standard units, where applicable.

It is recommended that authors do not use abbreviations in the title and limit their use in the abstract and in the text.

The generic names should be used for all drugs. The drugs can be referred to by their trade name, however, the manufacturer's name, city and country or electronic address should be stated in brackets in the Materials and Methods section.

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ORGANIZING THE ELECTRONIC FILE: All parts of the manuscript should be included in a single file. It should be formed by the cover page, then the text, references, figures (with their captions) and finally, tables and charts (with their respective captions).

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d) The place where the work was performed;
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CONCLUSION: The conclusion should be clear and concise, establishing a link between the conclusion and the study objectives. Avoiding conclusions not based on data from the study in question is recommended, as well as avoiding suggest that studies with larger samples are needed to confirm the results of the work in question.

ACKNOWLEDGEMENTS

When applicable, briefly acknowledge the people who have contributed intellectually or technically to the study, but whose contribution does not justify co-authorship. The author must ensure that people agree to have their names and institutions disclosed. Financial support for the research and fellowships should be acknowledged in this section (funding agency and project number).

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Ex.: Enzensberger W, Fisher PA. Metronome in Parkinson's disease [abstract]. Lancet. 1996;34:1337.

e) Personal communications: should only be mentioned in the text, between parentheses.

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Levels of Evidence for Primary Research Question[a]

(This chart was adapted from material published by the Centre for Evidence-Based Medicine, Oxford, UK. For more information, please visit www.cebm.net.)

	Types of study			
Level	**Therapeutic Studies Investigating the Results of Treatment**	**Prognostic Studies - Investigating the Effect of a Patient Characteristic on the Outcome of Disease**	**Diagnostic Studies - Investigating a Diagnostic Test**	**Economic and Decision Analyses - Developing an Economic or Decision Model**
I	High quality randomized trial with statistically significant difference or no statistically significant difference but narrow confidence intervals	High quality prospective study[d] (all patients were enrolled at the same point in their disease with ≥80% of enrolled patients)	Testing of previously developed diagnostic criteria on consecutive patients (with universally applied reference ''gold'' standard)	Sensible costs and alternatives; values obtained from many studies; with multiway sensitivity analyses
	Systematic review[b] of Level RCTs (and study results were homogenous[c])	Systematic review[b] of Level I studies	Systematic review[b] of Level I studies	Systematic review[b] of Level I studies
II	Lesser quality RCT (eg, < 80% followup, no blinding, or improper randomization)	Retrospective[f] study	Development of diagnostic criteria on consecutive patients (with universally applied reference ''gold'' standard)	Sensible costs and alternatives; values obtained from limited studies; with multiway sensitivity analyses
	Prospective[d] comparative study[e]	Untreated controls from an RCT	Systematic review[b] of Level II studies	Systematic review[b] of Level II studies
	Systematic review[b] of Level II studies or Level I studies with inconsis tent results	Lesser quality prospective study (eg, patients enrolled at different points in their disease or <80% followup)		
		Systematic review[b] of Level II studies		
III	Case control study[g]	Case control study[g]	Study of non consecutive patients; without consistently applied reference ''gold'' standard	Analyses based on limited alternatives and costs; and poor estimates
	Retrospective[f] comparative study[e]		Systematic review[b] of Level III studies	Systematic review[b] of Level III studies
	Systematic review[b] of Level III studies		Case-control study	
			Poor reference standard	
IV	Case series[h]	Case series		Analyses with no sensitivity analyses
V	Expert opinion	Expert opinion	Expert opinion	Expert opinion

[a] A complete assessment of quality of individual studies requires critical appraisal of all aspects of the study design.

[b] A combination of results from two or more prior studies.

[c] Studies provided consistent results.

[d] Study was started before the first patient enrolled.

[e] Patients treated one way (eg, cemented hip arthroplasty) compared with a group of patients treated in another way (eg, uncemented hip arthroplasty) at the same institution.

[f] The study was started after the first patient enrolled.

[g] Patients identified for the study based on their outcome, called "cases" eg, failed total arthroplasty, are compared with patients who did not have outcome, called ''controls'' eg, successful total hip arthroplasty.

[h] Patients treated one way with no comparison group of patients treated in another way.

EDITORIAL

A *Acta Ortopédica Brasileira* completa 25 anos de existência. Durante esse período, o principal objetivo do periódico foi contribuir para a disseminação do conhecimento científico de qualidade na área de Ortopedia junto à comunidade médica e científica nacional e internacional.

Quando foi iniciado o projeto da nossa revista Acta Ortopédica Brasileira, era inimaginável, mesmo no mais otimista dos cenários, que ela alcançasse o patamar em que se encontra hoje. Seu reconhecimento por vários dos mais importantes indexadores científicos do mundo reflete a alta qualidade da produção científica da Ortopedia Brasileira, fruto do trabalho de todos os membros do Conselho Editorial, assim como dos pesquisadores que colaboraram ao longo destes 25 anos e confiaram na publicação para a divulgação de sua produção. A Acta hoje integra a base SciELO, e está indexada no PubMed, Web of Science, PubMEd Central, Scopus, Redalyc, LILACS e DOAJ.

Como editores da *Acta Ortopédica Brasileira* sempre nos dedicamos ao ensino e à pesquisa acadêmica como, trabalho de extrema importância que exercemos voluntariamente, em prol do fortalecimento dos periódicos brasileiros e da valorização da pós-graduação *stricto sensu* na área da Ortopedia, sempre priorizando as publicações frutos dos programas de mestrado e doutorado acadêmicos brasileiros.

Continuaremos a buscar a excelência do trabalho editorial para que o periódico possa representar a pesquisa científica do Brasil na área de Ortopedia com a qualidade e os requisitos de indexadores internacionais.
Esperamos continuar com o inestimável apoio e colaboração de todos os docentes de nosso Corpo Editorial, sem os quais nenhum de nossos objetivos teria sido alcançado.

Olavo Pires de Camargo
Editor -Chefe

Tarcisio Eloy Pessoa de Barros Filho
Editor Emérito

OSTEOBAN
ibandronato de sódio

Segurança na prevenção e tratamento da Osteoporose.[1,2]

Detalhes que fazem a diferença no combate à Osteoporose[1,5,6,7]

Prevenção:
- **34% de redução de risco** de fraturas não vertebrais.*[3]
- **Redução de risco** de fraturas vertebrais.*[4]

Eficácia:
Melhora da **densidade mineral óssea** em mulheres com osteopenia e osteoporose.[5]

Comodidade:
Posologia cômoda: **1x ao mês.[1]**

* Refere-se ao ibandronato de tratamento diário

CUIDADOS PELA VIDA | Benefícios para uma vida melhor.

Referências Bibliográficas:1) Bula do produto OSTEOBAN: comprimido revestido. Farmacêutica Responsável: Gabriela Mallmann. Guarulhos, SP. Aché Laboratórios Farmacêuticos S.A. 2) BUMBASIREVIC, M. et al. Prospective clinical study of monthly ibandronate in the treatmetn of osteoporosis and prevention of fractures in postmenopausal women: ORPHEUM study. Srp Arh Celok Lek, v. 139, n. 11-12, p. 790-7694, 2011. 3) MILLER, P. D. et al Efficacy of monthly oral ibandronate is sustained over 5 years: the MOBILE long-term extension study. Osteoporos Int, v. 23, n. 6, 2012. 4) HARRIS, S. T. et al. Ibandronate and the risk of nonvertebral and clinical fractures in women with postmenopausal osteoporosis: results of a metaanalysis of phase III studies. Curr Med Res Opin, v. 24, n. 1, p. 237-245, 2008. 5) BOCK, O. et al. Impact of oral ibandronate 150 mg once monthly on bone structure and density in post-menopausal osteoporosis or osteopenia derived from in vivo ?CT. Bone, v. 50, p. 317-324, 2012. 6) Kairos Web Brasil. Disponível em: < http:// brasil.kairosweb.com>. Acesso em: Jul/ 2016. 7) Programa Cuidados pela Vida (O Programa Cuidados pela Vida pode alterar ou interromper esta campanha sem aviso prévio. Desconto calculado sobre o Preço Máximo ao Consumidor).

Interação Medicamentosa: Os pacientes devem esperar 60 minutos após ingerir OSTEOBAN, antes de tomarem outros medicamentos orais. Contraindicação: OSTEOBAN é contraindicado a pacientes que não conseguem ficar em pé ou sentados durante, pelo menos, 60 minutos.

Osteoban. ibandronato de sódio 150mg comprimido revestido. USO ORAL USO ADULTO. Indicações: OSTEOBAN é indicado para o tratamento da osteoporose pós-menopausa, com a finalidade de reduzir o risco de fraturas vertebrais. Em um subgrupo de pacientes de risco, com escore T < -3,0 DP no colo do fêmur, ibandronato de sódio também demonstrou reduzir o risco de fraturas não vertebrais. **Contraindicações**: **OSTEOBAN é contraindicado a pacientes com hipersensibilidade ao ibandronato de sódio ou aos demais componentes da fórmula e a pacientes com hipocalcemia não corrigida; pacientes com anormalidades do esôfago, como demora no esvaziamento esofágico, estenose ou acalasia; pacientes que não conseguem ficar em pé ou sentados durante, pelo menos, 60 minutos. Precauções e advertências: OSTEOBAN é contraindicado a pacientes com hipocalcemia não corrigida. Bisfosfonatos administrados por via oral podem causar irritação local da mucosa gastrintestinal superior. O risco de experiências adversas esofágicas graves parece ser maior para pacientes que não seguem as instruções de uso e/ou que continuaram a tomar bisfosfonatos por via oral após desenvolver sintomas sugestivos de irritação esofágica. Os pacientes devem prestar especial atenção e serem capazes de cumprir as instruções de administração. Considerando-se que anti-inflamatórios não esteróides e bisfosfonatos associam-se, ambos, à irritação gastrintestinal, recomenda-se cautela durante a administração concomitante de anti-inflamatórios não esteroides e ibandronato de sódio. Osteonecrose de mandíbula foi relatada em pacientes tratados com bisfosfonatos. A maioria dos casos em pacientes oncológicos submetidos a procedimentos dentários, mas alguns casos ocorreram em pacientes em tratamento para osteoporose pós-menopausa e outros diagnósticos. Fatores de risco conhecidos para osteonecrose de mandíbula: câncer, terapias concomitantes (ex: quimioterapia, radioterapia e corticosteroides) e distúrbios concomitantes (ex: anemia, coagulopatia, infecção e doença dentária pré-existente). A maioria dos casos foi relatada em pacientes tratados com bisfosfonatos de administração intravenosa, mas também em alguns pacientes tratados com bisfosfonatos orais.Relatos na literatura médica indicam que os bisfosfonatos podem estar associados à inflamação ocular, como uveíte e esclerite. Não foram realizados estudos sobre os efeitos de ibandronato de sódio sobre a capacidade de dirigir veículos e operar máquinas. Gestação e lactação: Categoria de risco na gravidez: B. Este medicamento não deve ser utilizado por mulheres grávidas sem orientação médica ou do cirurgião-dentista.** Não há experiência sobre o uso clínico de ibandronato de sódio em mulheres durante a gestação. OSTEOBAN não deve ser utilizado por mulheres que estejam amamentando sem orientação médica ou do cirurgião dentista. **Atenção diabéticos: contém açúcar (lactose). Interações medicamentosas:** é provável que suplementos à base de cálcio, antiácidos e alguns medicamentos orais que contenham cátions multivalentes (tais como alumínio, magnésio e ferro) interfiram na absorção de ibandronato de sódio. Os pacientes devem esperar 60 min após ingerir OSTEOBAN, antes de tomarem outros medicamentos orais. Foi demonstrada, em estudo de interação farmacocinética em mulheres na pós-menopausa, a ausência de qualquer interação potencial com tamoxifeno ou tratamentos de reposição hormonal (estrogênio). Não se observou interferência quando ibandronato de sódio foi administrado concomitantemente com melfalano / prednisolona em pacientes com mieloma múltiplo. **Interações com alimentos:** a ingestão de alimentos deve ser postergada em 60 min após a administração oral de ibandronato de sódio. **Reações adversas: reações adversas comuns (> 1/100 e ≤ 1/10): doença do refluxo gastroesofágico, diarreia, dor abdominal, dispepsia, náusea, flatulência, cefaleia, síndrome influenza-like, fadiga, artralgia, mialgia, exantema. Reação incomum (>1/1.000 e <1/100):** distúrbios gastrintestinais (gastrite, esofagite, incluindo ulcerações esofágicas ou estenose, vômitos e disfagia), distúrbios do sistema nervoso (tonturas), distúrbios musculoesqueléticos e do tecido conjuntivo (dor nas costas). **Reação rara (>1/10.000 e <1/1.000):** distúrbios gastrintestinais (duodenite), distúrbios do sistema imunológico (reações de hipersensibilidade), distúrbios da pele e do tecido subcutâneo (angioedema, edema facial e urticária). **Posologia** deve ser administrado em jejum, 60 min antes da ingestão do primeiro alimento ou bebida do dia (exceto água) e antes da administração de qualquer outro medicamento ou suplemento, inclusive cálcio. Os comprimidos devem ser deglutidos inteiros, com um copo cheio de água filtrada (180 a 240 mL). O paciente não deverá deitar-se nos 60 min seguintes após tomar o medicamento; A dose recomendada de OSTEOBAN é um comprimido de 150 mg, **uma vez por mês**. **Pacientes idosos:** não é necessário ajuste de dose. **Pacientes com insuficiência renal:** não é necessário ajuste de dose para pacientes com insuficiência renal leve a moderada e com depuração de creatinina ≥ 30 mL/min. Em pacientes com depuração de creatinina < 30 mL/min, a decisão de administrar OSTEOBAN deve ser baseada na avaliação individual da relação risco / benefício. **Pacientes com insuficiência hepática:** não há necessidade de ajuste de dose para pacientes com insuficiência hepática. "SE PERSISTIREM OS SINTOMAS, O MÉDICO DEVERÁ SER CONSULTADO." **VENDA SOB PRESCRIÇÃO MÉDICA**. MS - 1.0573.0422. **"Material técnico científico de distribuição exclusiva a profissionais de saúde habilitados à precrição e/ou dispensação de medicamentos"**. 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SUMMARY

VOLUME 25–Nº 1–2017

Original Articles

SPINE

OSTEOMETABÓLIC DISEASES

KNEE

SHOULDER

FOOT AND ANKLE

Systematic Review Article

HAND

REFERÊNCIAS BIBLIOGRÁFICAS: 1) IOLASCON, G. et al. Risendronate's efficacy: from randomized clinical trials to real clinical practice. Clinical Cases in Mineral and Bone Metabolism, v. 7, n. 1, p. 19-22, 2010. 2) BRASIL. ANVISA. Agência Nacional de Vigilância Sanitária. Resolução - RE nº 1.101, de 9 de abril de 2015. Concede Certificação de Boas Práticas de Fabricação ao Aché. Diário Oficial da União, Brasília, DF, P. 133, 9 abril 2015. 3) Kairos Web Brasil. Disponível em: http://brasil.kairosweb.com. Acesso em: Jun/2016. 4) Programa Cuidados pela Vida (O Programa Cuidados pela Vida pode alterar ou interromper esta campanha sem aviso prévio. Desconto calculado sobre o Preço Máximo ao Consumidor).

CONTRAINDICAÇÕES: OSTEOTRAT está contraindicado em pacientes com hipersensibilidade a qualquer componente da fórmula, com hipocalcemia, durante a gravidez, lactação e para pacientes com insuficiência renal severa ("clearance" de creatinina < 30 mL/min). INTERAÇÕES MEDICAMENTOSAS: Não foram realizados estudos formais de interação medicamentosa, entretanto, durante os estudos clínicos não foi observada qualquer interação clinicamente relevante com outros medicamentos.

OSTEOTRAT. risedronato sódico 35 mg. comprimidos revestidos. USO ORAL. USO ADULTO. Indicações: tratamento e prevenção da osteoporose em mulheres no período pós-menopausa para reduzir o risco de fraturas vertebrais e não vertebrais. Tratamento da osteoporose em homens com alto risco de fraturas. **Contraindicações: hipersensibilidade a qualquer componente da fórmula, hipocalcemia, gravidez e lactação e para pacientes com insuficiência renal severa ("clearance" de creatinina <30 mL/min), Precauções e advertências: Alimentos, bebidas (exceto água) e drogas contendo cátions polivalentes (tais como: cálcio, magnésio, ferro e alumínio) podem interferir na absorção dos bisfosfonatos e não devem ser administrados concomitantemente. Em mulheres mais idosas (> 80 anos), a evidência de manutenção da eficácia de risedronato sódico, é limitada. Alguns bisfosfonatos foram relacionados a esofagites e ulcerações esofágicas. Em pacientes que apresentam antecedentes de alteração esofágica que retardam o trânsito ou o esvaziamento esofágico (ex. estenosose ou acalasia), ou que são incapazes de permanecerem em posição ereta por pelo menos 30 minutos após a ingestão do comprimido, o risedronato deve ser utilizado com especial cautela. Os prescritores devem enfatizar a importância das instruções posológicas para pacientes que apresentam antecedentes de alterações esofágicas. A hipocalcemia deve ser tratada antes do início do tratamento com OSTEOTRAT. Outras alterações ósseas e do metabolismo devem ser tratadas quando iniciada a terapia com OSTEOTRAT.** Osteonecrose de mandíbula, geralmente associada com extração dentária e/ou infecção local foi relatada em pacientes com câncer em regimes de tratamento com bisfosfonatos, principalmente, na administração intravenosa. Osteonecrose de mandíbula também foi relatada em pacientes com osteoporose recebendo bisfosfonatos orais. Este medicamento contém lactose. Pacientes com problemas hereditários raros de intolerância à galactose, a deficiência da Lapp lactaseou má absorção da glucose-galactose, não devem tomar esse medicamento. Gravidez e lactação: O risco potencial para humanos é desconhecido. Risedronato sódico só deve ser utilizado durante a gravidez, se o risco benefício justificar o potencial risco para a mãe e o feto. A decisão de descontinuar a amamentação ou o produto deve considerar a importância do medicamento para mãe. Interações medicamentosas: Se considerado apropriado, OSTEOTRAT pode ser utilizado concomitantemente com a terapia de reposição hormonal. A ingestão concomitante de medicamentos contendo cátions polivalentes (ex. cálcio, magnésio, ferro e alumínio) irá interferir na absorção de OSTEOTRAT. O uso concomitante de antiácidos pode reduzir a absorção de risedronato. OSTEOTRAT não é metabolizado sistemicamente, não induz as enzimas do citocromo P450 e apresenta baixa ligação protéica. **Reações adversas: Estão listadas a seguir de acordo com a seguinte convenção: muito comum (>1/10); comum (>1/100; <1/10); incomum (>1/1000; <1/100); raro (>1/10000; <1/1000); muito raro (<1/10000). Comuns: dor de cabeça, constipação, dispepsia, náusea, dor abdominal, diarréia, dor musculoesquelética. Incomuns: gastrite, esofagite, disfagia, duodenite, úlcera esofágica Raros: glossite, estenose esofágica. Muito raramente foram observadas reações como: uveíte, irite, osteonecrose de mandíbula, hipersensibilidade e reações cutâneas, incluindo angioedema, rachaduras generalizadas e reações bolhosas de pele, algumas severas. Raramente observaram-se anormalidades nos testes de função hepática. Relatos laboratoriais: foram observados em alguns pacientes discreta diminuição nos níveis de cálcio sérico e fosfato, as quais foram precoces, transitórias e assintomáticas. Posologia**: A dose recomendada nos adultos é de 1 comprimido de 35 mg uma vez por semana, por via oral. Deve ser administrado no mínimo 30 minutos antes da primeira refeição, outra medicação ou bebida (exceto água) do dia. Os comprimidos devem ser engolidos inteiros, sem deixá-los dissolvendo na boca ou mastigá-los. Os pacientes devem utilizar OSTEOTRAT enquanto estiverem na posição vertical, com um copo de água (120 mL) para auxiliar a chegada ao estômago. Os pacientes não devem deitar por 30 minutos após ingestão de OSTEOTRAT. O comprimido de Osteotrat deve ser tomado no mesmo dia de cada semana, não devem ingeridos dois comprimidos no mesmo dia. Nenhum ajuste de dose é necessário para pacientes com insuficiência renal leve a moderada. O uso do risedronato sódico é contraindicado em pacientes com insuficiência renal severa ("clearance" de creatinina menor que 30 mL/min.) "SE PERSISTIREM OS SINTOMAS, O MÉDICO DEVERÁ SER CONSULTADO." VENDA SOB PRESCRIÇÃO MÉDICA. MS - 1.0573.0418. 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Material técnico científico de distribuição exclusiva à classe médica.

MOTORE
Curcuma longa 250 mg

O ANTI-INFLAMATÓRIO
COMPROVADAMENTE[3] EFICAZ E SEGURO
A LONGO PRAZO[1]

EXTRATO DE CURCUMINA COMPLEXADO
TECNOLOGIA **EXCLUSIVA**[3,4]

Exclusivo complexo curcumina-fosfatidilcolina (fitossomo):
18X mais biodisponível
em comparação à curcumina não complexada.[3]

Cientificamente comprovado
Curcumina principal fração (curcuminoide) com ação anti-inflamatória amplamente estudada.[3]

Referências Bibliográficas: 1) BELCARO, G et al: Efficacy and Safety of Meriva®, a Curcumin-phosphatidylcholine Complex,during Extended Administration in Osteoarthritis Patients. Alternative Medicine Review 15(4):337-344,2010. 2) BOSI,PL: saúde baseada em evidências. disponível em: http://disciplinas.nucleoead.com.br/pdf/Livro_SaudeBaseadaemEvidencias.pdf. Acesso em 11/2015. 3) JURENKA, S. J. Anti-inflammatory properties of Curcumin, a major constituent of Curcuma longa: a review of preclinical and clinical research. Alternative Medicine Review, v.14, n.2, p. 141-153, 2009. 4) CUOMO, J. et al. Comparative absorption of a standardized curcuminoid mixture and its lecithin formulation. J Nat Prod, v.74, p.664-669, 2011. 5) Bula do produto MOTORE: cápsulas. Responsável Técnico: Gabriela Mallmann. Guarulhos, SP. Aché Laboratórios Farmacêuticos S.A.

Contraindicações: contraindicado em caso de alergia à curcumina, açafrão *(Curcuma longa)* ou a qualquer outro componente da fórmula. É contraindicado em pacientes que estejam em tratamento com medicações que alterem as características de coagulação como antiagregantes plaquetários, anticoagulantes, heparina de baixo peso molecular e agentes trombolíticos. É também contraindicado em casos onde haja risco de obstrução de vias biliares ou casos de cálculos biliares, úlceras estomacais e hiperacidez do estômago.

MOTORE curcuma longa Extrato seco. **Cápsulas 250 mg. USO ORAL. USO ADULTO. Indicações**: medicamento fitoterápico destinado ao tratamento da osteoartrite e artrite reumatóide, e tem ação antiinflamatória e antioxidante. **Cuidados e advertências: a curcumina é muito bem tolerada em seu uso por via oral pela grande maioria dos pacientes, sendo raros os relatos de efeitos prejudiciais. Raramente podem ocorrer queixas como desconforto gástrico leve e movimentos intestinais mais frequentes. Precauções e advertências: o uso da curcumina por via oral mostrou ser bem tolerada pela maioria dos pacientes. Em casos esporádicos foram relatados episódios de menor gravidade como desconforto gastrointestinal. Não há relatos de overdose ou efeito tóxico grave. Em caso de ocorrência de reação de hipersensibilidade, a medicação deve ser imediatamente descontinuada e os sintomas avaliados pelo médico. Motore deve ser tomado apenas por via oral. Os riscos do uso por via de administração não recomendada são a não obtenção do efeito desejado e a ocorrência de reações adversas indesejadas. Não há dados de segurança relativo ao uso da curcumina em portadores de insuficiência hepática e/ou renal, não sendo recomendável o uso da medicação em pacientes nessas condições. As doses de tratamento recomendadas não devem ser excedidas. Informe ao seu médico ou cirurgião-dentista se você está fazendo uso de algum outro medicamento. Não use medicamento sem o conhecimento do seu médico. Pode ser perigoso para a sua saúde. Gravidez e lactação:** apesar de não haver estudos conclusivos em humanos que mostrem efeito negativo na fertilidade humana, alguns estudos realizados em animais sinalizaram efeito negativo na implantação de embriões após uso injetável de altas doses de extrato etanol da curcuma. Desta maneira sugere-se evitar o uso da curcumina em pacientes com intenção de engravidar ou em gestantes. Mulheres em fase de lactação também devem evitar o uso desta medicação. Categoria de risco na gravidez C: Este medicamento não deve ser utilizado por mulheres grávidas sem orientação médica ou do cirurgião-dentista. **Interações medicamentosas: é contraindicado para uso em pacientes que estejam fazendo uso de medicações que alterem as características de coagulação como antiagregantes plaquetários, anticoagulantes, heparina de baixo peso molecular e agentes trombolíticos, pois, pode haver aumento no risco de casos de sangramento. Reações adversas: o uso da curcumina por via oral mostrou ser bem tolerada pela maioria dos pacientes. Em casos esporádicos foram relatados episódios de menor gravidade como desconforto gastrointestinal. Não há relatos de overdose ou efeito tóxico grave.** Em caso de ocorrência de reação de hipersensibilidade, a medicação deve ser imediatamente descontinuada e os sintomas avaliados pelo médico. Motore deve ser tomado apenas por via oral. Os riscos do uso por via de administração não recomendada são a não obtenção do efeito desejado e a ocorrência de reações adversas indesejadas. Não há dados de segurança relativo ao uso da curcumina em portadores de insuficiência hepática e/ou renal, não sendo recomendável o uso da medicação em pacientes nessas condições. As doses de tratamento recomendadas não devem ser excedidas. **Posologia:** Motore deve ser ingerido por via oral, com um pouco de água. A dose habitual para adultos é de 2 cápsulas a cada 12 (doze) horas, ou seja, duas tomadas diárias, totalizando 500mg de medicação a cada tomada. "SE PERSISTIREM OS SINTOMAS, O MÉDICO DEVERÁ SER CONSULTADO." **VENDA SOB PRESCRIÇÃO MÉDICA.** MS - 1.0573.0442. **MB 03 SAP 4437701.**

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TOMOGRAPHIC MORPHOLOGICAL STUDY OF THE CRANIUM AND ITS CORRELATION WITH CRANIAL HALO USE IN ADULTS

ESTUDO MORFOLÓGICO TOMOGRÁFICO DO CRÂNIO E SUA CORRELAÇÃO COM O EMPREGO DO HALO CRANIANO EM ADULTOS

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ABSTRACT

Objective: To evaluate using tomographic study the thickness of the cranial board at the insertions points of the cranial halo pins in adults. Methods: This is a retrospective, cross-sectional, descriptive analysis of Computed Tomography (CT) scans of adult patients' crania. The study included adults between 20 and 50 years without cranial abnormalities. We excluded any exam with cranial abnormalities. Results: We analyzed 50 CT scans, including 27 men and 23 women, at the original insertion points and alternative points (1 and 2 cm above the frontal and parietal bones). The average values were 7.4333 mm in the frontal bone and 6.0290 mm in the parietal bone. Conclusion: There was no statistically significant difference between the classical and alternative points, making room for alternative fixings and safer introduction of the pins, if necessary. ***Level of Evidence II, Retrospective Study.***

Keywords: Spine. Traction. Skull.

RESUMO

Objetivo: Avaliar, através de estudo tomográfico, a espessura da tábua craniana nos pontos de inserção dos pinos do halo craniano em adultos. Métodos: Trata-se de estudo retrospectivo de corte transversal de análise de exames de tomografia computadorizada de crânios de pacientes adultos. Foram incluídos adultos entre 20 e 50 anos sem anormalidades cranianas. Excluiu-se qualquer anormalidade craniana. Resultados: Analisamos 50 tomografias de 27 homens e 23 mulheres nos pontos originais de inserção e em pontos alternativos, 1 e 2 cm acima, nos ossos frontal e parietal. Os valores médios encontrados foram de 7,4333 mm no osso frontal e 6,0290 mm no osso parietal. Conclusão: Não constatamos diferença estatisticamente significativa entre os pontos clássicos e os alternativos, abrindo espaço para fixações alternativas e introdução mais segura dos pinos, em caso de necessidade. ***Nível de Evidência II, Estudo Retrospectivo.***

Descritores: Coluna vertebral. Tração. Crânio.

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INTRODUCTION

The cranial halo is a versatile cervical traction method that can be used in a variety of circumstances.[1] Its use was first reported by Nickel et al.;[2] this method is most commonly used to reduce or realign fractures or dislocations of the cervical spine.[1] Other applications include severe scoliosis requiring fusion, osteotomies, or arthrodesis fusion.[3-5]

Complications of the cranial halo include infection of the pin insertion site (20%),[1,6,7] loosening of the screws (36%),[1,6,7] and nerve damage at the pin trajectory,[1,6,7] which are for the most part caused by inappropriate insertion or poor halo placement technique.[1,6,7]

However, despite the problems described, the halo is an effective technique preferred in classic situations, and if it is applied correctly it carries a low risk of complications.[3]

Few anatomical studies and radiological findings in the scientific medical literature focus on analyzing the cranial measurements in the adult population. One fact which has received little study is the thickness between the internal and external tables of the skull where the pins of a cranial halo are inserted (internal-external table thickness, or IETT), which has not been well-determined in adults. This knowledge has clinical importance due to multiple complications described in the literature such as pin penetration through the internal table of the skull, for example.[1,8,9]

In this scenario, the objective of this study is to evaluate primary anatomical and tomographic parameters for the skull and establish a correlation with the use of the cranial halo in adult individuals. A second goal is to serve as a base for future clinical studies.

All the authors declare that there is no potential conflict of interest referring to this article.

Study conducted at Universidade de São Paulo, Faculdade de Medicina, Department of Orthopedics and Traumatology, Laboratório de Investigação Médica do Sistema Musculoesquelético, São Paulo, SP, Brazil.
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MATERIALS AND METHODS

This is a cross-sectional, retrospective study based on analysis of computed tomography (CT) scans of skulls of young adult patients aged 20–50 years. Scans performed over a period of 11 months (January 2, 2015–December 2, 2015) at the Institute of Radiology and Diagnostic Imaging at the Faculdade de Medicina da Universidade de São Paulo (INRAD-FMUSP) were evaluated. The 50 scans were performed in patients who met the inclusion criteria (age 20–50 years old). The objective of this study is to describe normal values for measuring the thickness between the internal and external table thickness (IETT) in patients aged 20–50 using the following exclusion criteria: cranial fracture leading to bone deformities, invasive surgical procedures, congenital malformations, deformities resulting from other pathologies such as thalassemia, sickle cell anemia, and osteoporosis, cancer with metastasis to the cranium or with impairment of bone mineralization (multiple myeloma, for example). It is important to stress that the CT scans were selected by convenience, and the clinical justifications for the scans were not known. However, with the exclusion criteria we sought to ensure that patients with possible anatomical changes were not selected. The study was approved by the IOT-FMUSP Institutional Review Board under process number 1,782,521.

The IETT was measured in the 50 selected scans using proprietary software in the bone window setting in the sagittal, coronal, and axial planes. (Figure 1) The measurements were obtained in the axial planes, and the coronal and sagittal planes were used to locate the necessary points. These points used were described in the classic technique for inserting the cranial halo pins (anterior pins positioned 1 cm above the eyebrows, in the transition from the medial third to the lateral edge of the eyebrows; posterior pins placed 1 to 2 cm above the ears, selecting a halo with the greatest possible symmetry with the largest cephalic diameter, maintaining the proper alignment,[1,2,6] and those located 1 cm and 2 cm above. Points below the classic insertion sites were not used as a result of technical incongruence for the procedure deriving from anatomical limitations (eye socket and the external acoustic meatus).

Throughout the text, the studied points are addressed as follows: classic pin insertion point on the right side of the frontal bone is called "Frontal R", and the corresponding pin on the left side is "Frontal L". Similarly, the points 1 cm and 2 cm above the classic points on the left and right were called "Frontal R1", "Frontal L1", "Frontal R2", and "Frontal L2". The classic pin insertion point in the parietal bone on the right is "Parietal R", and the corresponding point on the left is "Parietal L". Similarly, the points 1 cm and 2 cm above the classic points on the left and right were called "Parietal R1", "Parietal L1", "Parietal R2", and "Parietal L2", respectively.

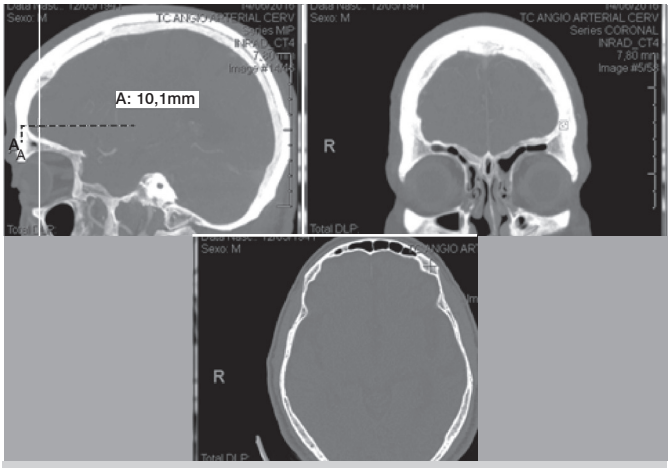

Figure 1. Location of the pin insertion point using line recognition in the sagittal plane and localization mode in the coronal plane provided by the software to measure the thickness of the internal and external tables of the skull, shown by the cross in the axial plane.

Analyses statistics

The data obtained were stored in an Excel for Mac spreadsheet. They were later exported to SPSS 23.0 for Mac software for statistical analysis of the data. Categorical data were described by their absolute number and their respective percentage. Continuous data (cranial thickness) were described by means and respective standard deviation. The right and left sides were compared using Student's t-test for paired samples. If the sides did not demonstrate significant differences, they were analyzed together to describe the thickness, which was demonstrated by a distribution curve to better visualize the percentile limits of the thicknesses of the sampled crania. Additionally, the data from different locations were analyzed using a non-parametric test because their distribution was not symmetrical, using the Kruskal-Wallis and Mann-Whitney tests. A type I error was considered when this value was below 5%.

RESULTS

We analyzed 50 CT scans from patients ranging in age from 22 to 46 years, comprising 27 men and 23 women. Average age at the time of the scan was 33.185 years for the men and 34.957 years for the women. (Figures 2 and 3).

Mean thickness at Frontal R was 7.5440 mm (minimum: 6.00 mm, maximum: 10.80 mm), with a standard deviation of 0.96429 mm. Mean thickness at Frontal R1 was 7.3460 mm (minimum: 5.80 mm, maximum 9.90 mm) with a standard deviation of 0.94095 mm. For Frontal R2, mean thickness was 7.3080 mm (minimum: 5.50 mm, maximum 9.90 mm) with a standard deviation of 0.93870 mm. (Table 1)

For the insertion points in the parietal bone, mean thickness at Parietal R was 6.0880 mm (minimum: 4.50 mm, maximum: 7.70 mm), with a standard deviation of 0.71390 mm. Mean thickness at Parietal R1 was 6.0060 mm (minimum: 4.50 mm, maximum 7.50 mm) with a standard deviation of 0.69764 mm. At Parietal R2, mean thickness was 5.9280 mm (minimum: 4.40 mm, maximum 7.60 mm) with a standard deviation of 0.72112 mm. (Figures 4–7)

Mean thickness at Parietal L was 6.1160 mm (minimum: 4.80 mm, maximum: 7.50 mm), with a standard deviation of 0.64027 mm. At Parietal L1, mean thickness was 6.0520 mm (minimum: 4.80 mm, maximum: 7.50 mm) with a standard deviation of 0.68935 mm. Finally, mean thickness at Parietal L2 was 5.9840 mm (minimum: 4.60 mm, maximum: 7.50 mm) with a standard deviation of 0.68463 mm. (Table 2)

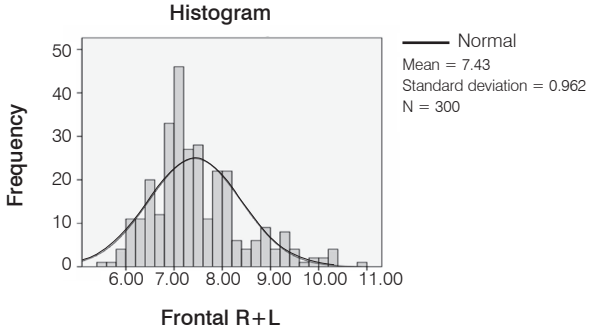

Figure 2. Distribution of the internal-external table thickness in the frontal bone in both sexes.

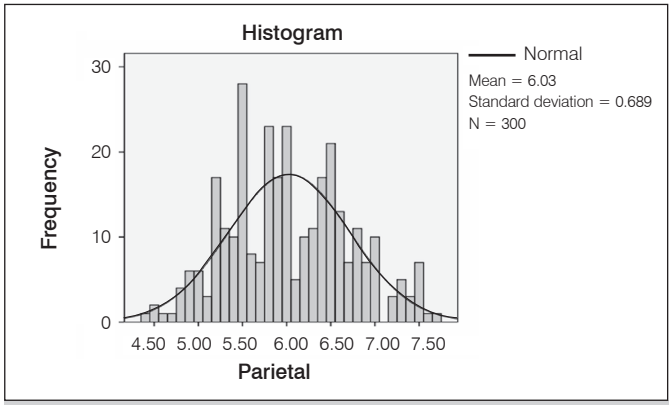

Figure 3. Distribution of the internal-external table thickness in the parietal bone in both sexes.

Table 1. IETT findings for the parietal bone in mm.

	N	Minimum (mm)	Maximum (mm)	Mean (mm)	Standard deviation
Frontal R	50	6.00	10.80	7.5440	0.96429
Frontal R1	50	5.80	9.90	7.3460	0.94095
Frontal R2	50	5.50	9.90	7.3080	0.93870
Frontal L	50	6.00	10.30	7.5900	0.98773
Frontal L1	50	6.00	10.30	7.4540	0.97984
Frontal L2	50	5.80	10.20	7.3580	0.97250
Valid N (listwise)	50				

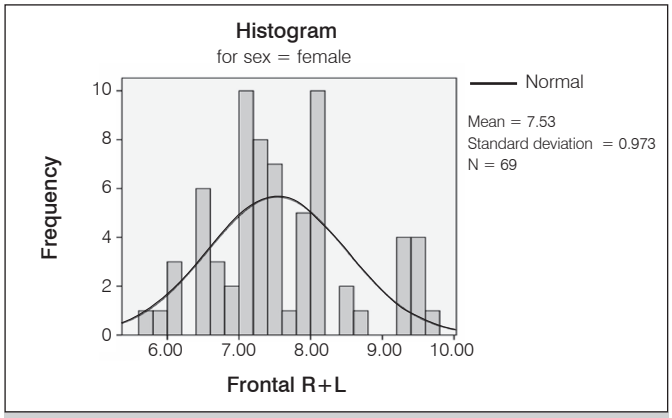

Figure 4. Distribution of the internal-external table thickness in the frontal bone in women.

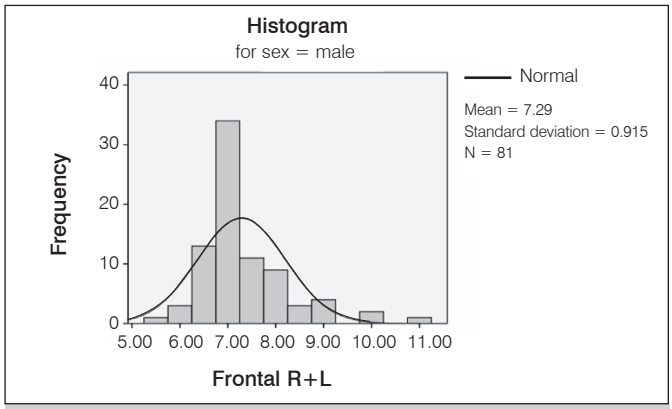

Figure 5. Distribution of the internal-external table thickness in the frontal bone in men.

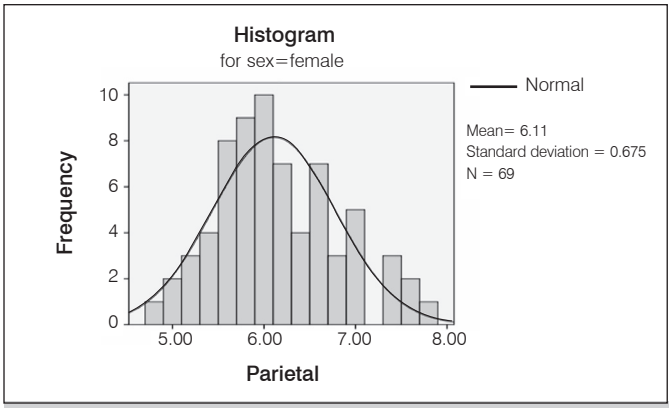

Figure 6. Distribution of the internal-external table thickness in the parietal bone in women.

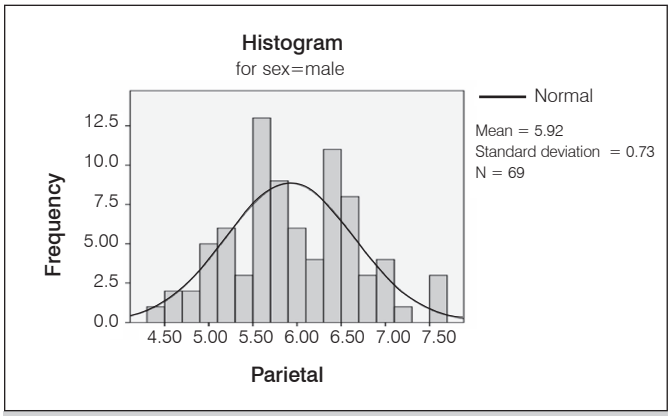

Figure 7. Distribution of the internal-external table thickness in the parietal bone in men.

Table 2. IETT findings for the parietal bone in mm.

	N	Minimum (mm)	Maximum (mm)	Mean (mm)	Standard Deviation
Parietal R	50	4.50	7.70	6.0880	0.71390
Parietal R1	50	4.50	7.50	6.0060	0.69764
Parietal R2	50	4.40	7.60	5.9280	0.72112
Parietal L	50	4.80	7.50	6.1160	0.64027
Parietal L1	50	4.80	7.50	6.0520	0.68935
Parietal L2	50	4.60	7.50	5.9840	0.68463
Valid N (listwise)	50				

DISCUSSION

The cranial halo and halo vest were used extensively in the past for definitive or temporary treatment of a wide variety of spine pathologies; in many centers, the halo vest remains the method of choice for treating conditions such as cervical spine trauma.[10] Classically, the halo is installed under sterile conditions in the surgical center according to the established positioning parameters, namely: (a) anterior pins positioned 1 cm above the eyebrows, in the transition from the medial third to the lateral edge; (b) posterior pins 1 to 2 cm above the ears, choosing a halo with the greatest possible symmetry with the largest cephalic diameter to maintain good alignment.[6]

Some studies found complications such as loosening of pins in up to 36% of cases. The most feared complication, dural puncture,

was seen in only 1% of cases.[6] Other serious complications such as pneumocranium, cerebral abscess, or epileptic seizures are rare.[7,11-13] Measurement and analysis of the thickness of the table of the skull showed no statistical difference between the frontal points evaluated in this study, and similarly no statistical difference was seen between the parietal points. However, it should be stressed that this was a pilot study that will serve as a foundation for further research on new insertion points for cranial halo pins in addition to skull mapping in order to prevent accidents and revise the cranial halo.

We found that the insertion of pins in the frontal bone must respect the mean measurement of 7.4333 mm; similarly, the mean measurement of 6.0290 mm in the parietal bone should also be observed in order to avoid inadvertent intracranial injury.

There was no statistical difference between the sexes in the frontal or the parietal bone, which is why the approach regarding length and insertion location remains the same for men and women. There was also no statistical difference between the original points of insertion and the points 1 and 2 centimeters above these original points in both the bones, affirming the current practice as the best option because of its long history, established installation practice, and the design of cranial halos.

Although we did not find differences, we should emphasize that this study is a pilot for future research, especially because of the lack of research on skull thickness in adults and children. Mapping the thickness of the tables of the skull will permit more objective pin insertion and increase the designation of alternative points for halo revision, factors that can decrease the risk of accidents during halo installation and repositioning.

CONCLUSION

There was no statistical difference between the thickness of the points evaluated in the frontal bone, nor between the points in the parietal bone. Both the original parameters as well as the studied alternatives for cranial halo insertion pins were proven to be viable options from an anatomical point of view in cases when revision is needed or soft tissue injury is present at the insertion site.

AUTHORS' CONTRIBUTIONS: Each author contributed individually and made significant contributions to the development of this manuscript. TFA (0000-0001-6188-280X)*, HTC (0000-0002-1551-4982)*, OBL (0000-0002-2614-1771)*, AFC (0000-0002-7797-5274)*, and RMM (0000-0001-5958-5646)* were responsible for drafting the manuscript. FFA (0000-0002-0746-265X)* contributed to the literature review, as well as the final revision of the manuscript. *ORCID (Open Researcher and Contributor ID).

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ROLE OF DIFFERENT HORMONES IN THE PATHOGENESIS AND SEVERITY OF ADOLESCENT IDIOPATHIC SCOLIOSIS

PAPEL DE DIFERENTES HORMÔNIOS NA PATOGÊNESE E GRAVIDADE DA ESCOLIOSE IDIOPÁTICA DO ADOLESCENTE

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ABSTRACT

Objective: To evaluate the hormonal profile of patients with adolescent idiopathic scoliosis (AIS) and its relationship to the severity of the curvature and quality of life. Method: Patients with scoliosis (Cobb angle above 10°), of both genders, diagnosed after 10 years of age were included, excluding those who presented other condition that could lead to scoliosis. Serum levels of 25-hydroxyvitamin D (25-OHD), cortisol and gastrin were correlated with Cobb angle and quality of life, measured by the SRS-30 questionnaire. Results: The levels of 25-OHD decreased in 97% of patients. There was an inverse relationship between gastrin levels and quality of life ($p = 0.016$). Moreover, there was an inverse correlation between the value of Cobb angle and quality of life ($p = 0.036$). There were no changes in cortisol levels. There was no correlation between Cobb angle and any of the hormones measured. Conclusion: The patients had levels of 25-OHD diminished, strengthening the hypothesis of its involvement in the development of AIS. This study also suggests that increased gastrin levels may be associated with a worse quality of life in patients with AIS. ***Level of Evidence II, Diagnostic Study.***

Keywords: Scoliosis. Adolescent. Gastrin. Cortisol. Vitamin D.

RESUMO

Objetivo: Avaliar o perfil hormonal dos pacientes com escoliose idiopática do adolescente (EIA) e sua relação com a gravidade da curvatura e qualidade de vida. Método: Foram incluídos pacientes com escoliose (ângulo de Cobb acima de 10°), de ambos os sexos, diagnosticados após 10 anos de idade e foram excluídos aqueles que apresentassem outra condição que pudesse acarretar em escoliose. Os valores séricos da 25-hidroxivitamina D (25-OHD), cortisol e gastrina foram correlacionados com o ângulo de Cobb e a qualidade de vida, mensurada através do questionário SRS-30. Resultados: Os níveos de 25-OHD estavam reduzidos em 97% dos pacientes. Observou-se uma relação inversa entre níveis de gastrina e a qualidade de vida (p=0,016). Ademais, constatou-se correlação inversa entre o valor do ângulo de Cobb e a qualidade de vida (p=0,036). Não foram observadas alterações nos níveis de cortisol. Não houve correlação do ângulo de Cobb com o nível de nenhum dos hormônios dosados. Conclusão: Os pacientes apresentaram níveis de 25-OHD diminuídos, fortalecendo a hipótese da sua implicação no desenvolvimento da EIA. O presente estudo também sugere que o aumento dos níveis de gastrina possa estar relacionado com pior qualidade de vida nos pacientes com EIA. ***Nível de Evidência II, Estudo Diagnóstico.***

Descritores: *Escoliose. Adolescente. Gastrina. Cortisol. Vitamina D.*

Citation: Silva RT, Fernandes RJR, Ono AHA, Marcon RM, Cristante AF, Barros Filho TEP. Role of different hormones in the pathogenesis and severity of adolescent idiopathic scoliosis. Acta Ortop Bras. [online]. 2017;25(1):15-7. Available from URL: http://www.scielo.br/aob.

INTRODUCTION

Adolescent idiopathic scoliosis (AIS) is a three-dimensional deformity of the spine with an average prevalence of 3% of the population, affecting 8 women for each man with this disorder.[1,2] Although its exact pathogenesis has not yet been described, several authors defend a multifactorial etiology.[3,4] Genetic changes, hormone dysfunctions, and bone mineralization deficit are among the examples of theories which have been postulated.[4,5]

Previous studies have demonstrated alterations in bone growth in AIS as well as reduced bone mineral density in these patients, but have not clarified the pathophysiology of these changes in detail.[6] The same difficulties and uncertainties exist in relation to eating disorders and low body mass index found in patients with AIS.[7,8]

Several studies have evaluated the action of gastrin, a peptide hormone produced by G cells of the gastric antrum, in metabolism and bone quality.[9,10] Also considering the importance of 25-hydroxyvitamin D (25-OHD) and cortisol in bone metabolism, we seek to correlate the levels of these markers with AIS, the severity of the curve, and the results obtained using the SRS-30 questionnaire.

The primary objective of this study is to evaluate the hormone profile of patients with AIS and its relation to the severity of the curve and performance on the SRS-30 questionnaire and its domains.

All the authors declare that there is no potential conflict of interest referring to this article.

Study conducted at Universidade de São Paulo, Faculdade de Medicina, Department of Orthopedics and Traumatology, Laboratório de Investigação Médica do Sistema Musculoesquelético, São Paulo, SP, Brazil.
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MATERIALS AND METHODS

The study participants were selected from the outpatient spine clinic at the hospital where this study was conducted, read and signed the free and informed consent form. The study was approved by the Ethics Committee (CEP: 780,768). Patients of both sexes with scoliosis (Cobb angle >10° in the coronal plane in panoramic X-rays) diagnosed after 10 years of age were included. We excluded patients with any genetic syndrome, other relevant chronic diseases, or previous osteo-metabolic, muscle, or endocrinological disorders of any kind. We also excluded patients with personal history that could justify the scoliosis, such as trauma or tumors.

The Cobb angle was measured by one doctor who is an experienced spinal specialist, considering the first panoramic radiography of the spine taken after the patient began to be followed at the outpatient clinic.

We measured serum values of 25-hydroxyvitamin D (using chemical immunoassay), cortisol (using chemical immunoassay), and gastrin (using chemiluminescence).

All patients completed the SRS-30 quality of life questionnaire by the Scoliosis Research Society (SRS), which is composed of 30 questions divided into five domains (function/activity, self-image/appearance, pain, mental health, and satisfaction with management). Each question is scored from 1 (worst) to 5 (best). The maximum score possible is 150 points, and a higher score represents a better self-evaluation by the patient. (Table 1).

Statistical methodology

The data were stored in an Excel® for Mac spreadsheet and subsequently imported into SPSS 23® for Mac. Continuous data were described by means and their respective standard deviations and were tested for distribution using the Kolmogorov-Smirnov test. The Pearson correlation coefficient and Spearman's rank correlation were used to analyze the correlations. Up to 5% was accepted as a type I error.

Funding

The laboratory tests were performed in the clinical laboratory of the Instituto de Ortopedia do Hospital de Clínicas da Faculdade de Medicina da Universidade de São Paulo using this institution's resources. To measure the Cobb angle, X-rays solicited during the patients' routine care were used. No sponsorships or grants were obtained for this study or by the authors.

RESULTS

The study was conducted with 43 people, 36 female and seven male, with an average age of 15.3 years ± 2.49.

We noted that 25-OHD levels were low in 97% of patients, classifying them as having insufficiency or deficiency. No alterations were observed in the other tests. (Table 2).

An inverse correlation was noted between a low Cobb angle and the quality of life in the SRS-30 questionnaire. No significant relationships were observed between the Cobb angle and measured hormone levels. (Table 3).

An inverse relationship was also noted between low gastrin values and performance on the quality of life questionnaire (SRS–30). No significant relationships were seen between the values for the other hormones and quality of life assessment. (Table 4)

Table 1. Descriptive analysis of the quantitative variables of the study.

Variables	Mean ± SD	Median	Min-Max
Initial Cobb angle	57.65 ± 23.022	57.00	20 - 123
Quality of Life	67,00 ± 16,837	67,00	26 - 107
(SRS – 30)	67.00 ± 16.837	67.00	26 - 107
25-OHD (ng/mL)	19.40 ± 6.9	17.50	6 - 36
Gastrin (pg/mL)	35.33 ± 48.66	20.10	8 - 266
Cortisol (g/dL)	11.98 ± 7.95	10.10	4.5 - 48.4

DISCUSSION

Despite all the research about AIS, its exact pathophysiology is still unknown. From the clinical changes which were recognized and present in the patients with this disease, we attempted to evaluate their alleged causes and possible markers of severity.

Recent studies indicate an interaction between 25-OHD deficiency and development of AIS,[11,12] which was corroborated in our study: almost all of the patients (97%) had lower 25-OHD levels than expected. Considering the small number of studies suggesting a

Table 2. Descriptive analysis of the qualitative variables of the study and reference values.

Variable	Reference values	n (%)	95% CI
Gastrin (pg/mL)			
Decreased	Below 13	(13) 30.23	15.34 – 45.12
Normal	13 – 115	(26) 60.46	44.69 – 76.24
Increased	Above 115	(2) 4.65	0.57 – 15.81
Omitted	-	(2) 4.65	0.57 – 15.81
Cortisol (g/dL)			
Decreased	Below 5	(4) 9.30	7.61 – 34.25
Normal	5 – 25	(35) 81.39	68.60 – 94.19
Increased	Above 25	(2) 4.65	0.57 – 15.81
Omitted	-	(2) 4.65	0.57 – 15.81
25-OHD (ng/mL)			
Deficiency	Below 10	(3) 7	1.46 – 19.06
Insufficiency	10 – 30	(37) 86	74.53 – 97.57
Sufficiency	30 – 100	(1) 2.3	0.06 – 12.29
Omitted	-	-	-

Table 3. Relationship between Cobb angle and quantitative variables of the study.

Variables	Cobb angle		
	n	**Pearson correlation**	***p***
Quality of Life (SRS - 30)	43	-0.320	0.036*
25-OHD	42	0.045	0.779
	n	**Spearman's rank correlation coefficient**	***p***
Cortisol	41	0.274	0.083
Gastrin	41	0.152	0.342

$p < 0.05$

Table 4. Relationship between SRS-30 and measured hormones.

Variables	Quality of life (SRS - 30)		
	N	**Spearman's rank correlation coefficient**	***p***
Gastrin	41	-0.375*	0.016*
Cortisol	41	-0.136	0.398
25OHD	42	0.193	0.220

$p < 0.05$

correlation between 25-OHD and AIS, further studies are needed to support this hypothesis and to the reasons behind this variation. No relationship was observed between vitamin D levels and Cobb angle in this study, which contradicts the single study found in the literature that correlated the two variables and showed an inverse relationship.[12] Furthermore, no relationship was found between 25-OHD levels and quality of life assessment.

Recent studies in rats suggest that gastrin may assist in regulation of bone metabolism, and that higher gastrin levels may contribute to poorer bone quality.[9,10] Although gastrin is present at normal levels in most patients, we found a low inverse correlation between gastrin values and the SRS-30 score, which may indicate that the most serious cases have higher serum gastrin levels. Since this is the first study correlating scoliosis and gastrin levels, further studies are required to better clarify this finding.

The cortisol levels in the patients studied were predominantly in the normal range. No relationship was observed between cortisol levels and Cobb angle or SRS-30 performance, making it unlikely they are involved in developing AIS.

Quality of life assessment in spinal diseases is common practice and is necessary for patient management. The Scoliosis Research Society provides a questionnaire for this purpose, the SRS-30.[13,14] Some studies, however, did not find a relationship between the score on this instrument and Cobb angle, contrary to our findings in this study.

CONCLUSION

The study participants showed low serum 25 OHD values, strengthening the hypothesis that this vitamin is involved in the development of AIS, as the current literature indicates. The present study also suggests that increased gastrin may be related to poorer quality of life in patients with AIS. No alterations were observed in the serum cortisol levels.

AUTHORS' CONTRIBUTIONS: Each author contributed individually and made significant contributions to the development of this manuscript. RMM (0000-0001-5958-5646)*, AFC (0000-0002-7797-5274)*, and TEPBF (0000-0002-0819-7712)* were responsible for supervision and technical coordination of the study; AHAO (0000-0001-7718-5742)* was responsible for examining the X-rays. The other authors, RTS (0000-0003-4405-373X)* and RJRF (0000-0002-0693-8441),* were responsible for drafting the article, data collection, statistical analysis together with a qualified professional, and submission of the project. *ORCID (Open Researcher and Contributor ID).

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PARQVE: PROJECT ARTHRITIS RECOVERING QUALITY OF LIFE THROUGH EDUCATION: TWO-YEAR RESULTS

PARQVE, PROJETO ARTROSE RECUPERANDO QUALIDADE DE VIDA PELA EDUCAÇÃO: RESULTADOS EM DOIS ANOS

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ABSTRACT

Objective: To evaluate the effects of a multi-professional educational program in patients with knee osteoarthritis (KOA). Methods: Prospective randomized controlled trial with 195 KOA patients. One group was submitted to two-day lectures and received educational material about KOA (Class group), and the control group received the educational material only. Patients were evaluated at baseline, twelve and 24 months. At evaluation, patients answered pain and functional questionnaires (WOMAC, Lequesne, VAS and SF-36); reported the intensity of exercise per week; measured the body fat percentage, weight and height to estimate body mass index (BMI); and performed Timed Up & Go (TUG) and Five-Times-Sit-to-Stand (FTSST) tests. Results: The groups presented similar results in all time points with respect to pain (VAS and WOMAC pain), WOMAC, BMI and body fat percentage ($p>0.05$). The Class group exhibited improved function according to the Lequesne questionnaire, whereas the control group worsened ($p=0.02$) during follow-up ($p<0.02$). TUG ($p=0.01$) and FTSST ($p<0.001$) improved in the Class group. A higher percentage of patients in the Class group performed regular physical activity ($p=0.045$). Conclusions: The educational program with classes improved the consistency of physical activity and the subjective and objective function of patients with KOA. ***Level of evidence IA, Prospective Randomized Controlled Trial.***

Keywords: Osteoarthritis. Knee. Quality of life. Patient education as topic. Treatment outcome.

RESUMO

Objetivo: Avaliar o efeito de um programa educacional multiprofissional para pacientes com gonartrite. Métodos: Trata-se de um estudo prospectivo randomizado com 195 pacientes portadores de gonartrite. Um grupo recebeu material didático sobre osteoartrite (grupo Controle) e o outro grupo participou de dois dias de aulas práticas e teóricas sobre osteoartrite e também recebeu o material didático (grupo Aula). Os pacientes preencheram questionários para avaliar dor, função e qualidade de vida (WOMAC, Lequesne, EVA, SF-36) no momento da inclusão, e após 12 e 24 meses de seguimento. Nestes mesmos períodos, os pacientes tiveram calculados a percentagem de gordura e o índice de massa corpórea (IMC); realizaram os testes de senta e levanta (TSL) e "Timed-Up-and-Go" (TUG), além de responder perguntas sobre a intensidade da atividade física semanal realizada. Resultados: Os dois grupos não diferiram quanto aos resultados de dor, função (WOMAC), IMC e porcentagem de gordura corpórea ($p>0,05$). O grupo Aula melhorou e o Controle piorou a função pelo Lequesne ($p=0,02$) ao longo do tempo ($p<0,02$). O TUG ($p=0,01$) e o TSL ($p<0,001$) melhoraram principalmente no grupo Aula. Uma porcentagem maior de pacientes do grupo Aula aderiu à atividade física regular ($p=0,045$). Conclusão: O programa educacional com aulas melhora adesão à atividade física e a função subjetiva e objetiva dos pacientes com gonartrite. ***Nível de Evidência IA, Estudo Prospectivo Controlado e Randomizado.***

Descritores: *Osteoartrite. Joelho. Qualidade de vida. Educação de pacientes como assunto. Resultado do tratamento.*

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INTRODUCTION

The incidence of osteoarthritis (OA) is known to increase with longevity, obesity and low socioeconomic level.[1,2]

Obesity and longevity are increasing in Brazil.[3,4] Approximately 50.2% of Brazilians have no education or incomplete primary education,[5] and although the GDP per capita in Brazil was R$ 20,876,00 reais (roughly US $ 8,134.00 dollars) in 2015,[6] people who earned more than 10 times the minimum monthly wage (minimum wage being approximately US$ 300.00) represented only 3.1% of the employed population in the country in 2010.[5] Therefore, the number of patients with OA is expected to increase in Brazil. Thus, a program that aims to change the fate of OA patients by decreasing Body Mass Index (BMI), increasing physical activity and providing tools to enhance their quality of life is essential to alleviate such a burden to society.[7]

All the authors declare that there is no potential conflict of interest referring to this article.

Study conducted at Universidade de São Paulo, Faculdade de Medicina, Department of Orthopedics and Traumatology, Laboratório de Investigação Médica do Sistema Musculoesquelético, São Paulo, SP, Brazil.
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The optimal management of OA requires a combination of pharmacological and non-pharmacological modalities.[8] There are several reports of minor effects of educational programs on pain, function, time spent in gyms and weight loss.[8] A previous positive experience in a weekly educational program on patients with osteoporosis inspired the present proposal of two days of lectures and workshops about OA to patients with knee OA (KOA) that are reinforced by telephone calls. Our one-year results failed to show a relevant difference in the groups that received telephone calls.[8] Because these telephone calls were time-consuming, they were suspended in the second year. This study evaluated the two-year effects of a multi-professional conservative treatment for patients with KOA by comparing the offering of the educational program with or without classes by assessing the subjective pain, function and quality of life questionnaires and by objective measures of (BMI), percentage of body fat (PBF), functional tests and engagement in regular physical activity.

METHODS

This study was performed at the Department of Orthopedics and Traumatology, São Paulo, Brazil, after receiving approval from the Ethics Committee for the Analysis of Research Projects (CAPPesq) under protocol number 0622/11.

Clinical trials registration number: NCT01572051.

This was a prospective, randomized controlled trial. This study followed the guidelines of the CONSORT statements for randomized controlled trials and non-drug treatments.

The care providers included six orthopaedic surgeons, four psychologists, three social workers, one nutritionist, five occupational therapists, three physical therapists and two physical educators, all of whom were volunteers or staff at the Orthopaedic Institute, Hospital das Clínicas, University of São Paulo.

Patients had to meet the following criteria: outpatient aged 45 years or older with KOA according to the American College of Rheumatology clinical and radiological definition;[9] no rheumatoid arthritis or any rheumatologic disease other than OA; had received typical care for OA in the past six months; knee pain rated above 30 mm on a numerical scale and necessitating drug treatment without any neurological problems; and able to understand and provide informed consent. The exclusion criteria included undergoing surgery during the study that was not related to OA and would prevent daily regular exercises, participating in another program with nutritional education or engaging in another clinical trial. Patients who were not able to perform the functional tests at baseline were excluded only from the functional analysis.

Participants were patients undergoing typical care for the treatment of KOA at the Osteometabolic Diseases Group, Department of Orthopedics and Traumatology, Hospital das Clínicas, University of São Paulo. By January 2012, 306 patients were undergoing typical care for KOA as described.[7]

At enrolment, patients were asked to respond to the VAS (Visual Analogue Scale), WOMAC™, Lequesne, and SF-36 questionnaires and to assess the frequency and intensity of physical activity performed/week.[10-12] Weight, height, and seven skin folds were measured to calculate body mass index (BMI) and percentage of body fat (PBF). Patients were asked to perform timed up-and-go TUG and five times sit to stand FTSST tests.[13,14] All patients received a plain radiograph of their knees, including weight-bearing anterior-posterior, lateral and patellar axial views. Three orthopaedic surgeons examined all radiographs to classify the severity of OA according to Kellgren and Lawrence (K&L)[15] In case of disagreement between two surgeons, the third surgeon was decisive.

Participants were randomly allocated into eight subgroups (1 to 4, according to the intervals between days of lectures, and A and B, according to the use or absence of telephone calls) of 28 or 29 participants each. The Class group had six subgroups, named 1, 2, and 3, which had lectures one, two and three months apart, respectively, either with (A) or without (B) bimonthly telephone calls. Subgroup 4 (with (A) and without (B) bimonthly telephone calls) received the educational material only and formed the Control group. Patients in each Class subgroup were asked to come to the hospital on two specific Saturdays according to the intervals of each group to participate in the educational program.[7]

All participants received the written and video (DVD) information of the lectures given on the first day of class.[7] The DVD was 2 hours and 23 minutes long. Patients from subgroups 4A and 4B watched the DVD for the first time at the hospital. All patients were asked to read the text and/or watch the DVD at home at least three times.

The physicians called patients in subgroup A two months after the lecture and every other month until the 1-year reassessment to reinforce the information given in the educational program.

Twelve and 24 months after the final lecture or after receiving the educational material, the patients returned for evaluation, where the same assessments performed at baseline were repeated.

Sample

This was a pilot study to evaluate the effectiveness of a two-day program about OA with respect to the sole offering of educational material (booklet and DVD) with particular intervals between classes and telephone calls. The authors aimed for 30 patients in each subgroup.

Randomization was performed by a computer-generated program available at http://www.randmization.com/.

Blinding

There was no difference in the demographic information between the groups. Groups 1 to 3 received classroom instruction from all professionals and both audio-visual and written instructions, which group 4 also received. When signing the informed consent forms, the patients knew that the groups would differ according to the time between classes, lack of classes and telephone calls. Evaluators did not know to which group the patient belonged. Two main assistants scheduled appointments and classes, retrieved material, and plotted the questionnaires' results in Excel sheets.

Statistical analysis

The nominal characteristics were described for each group using the absolute and relative frequencies, and the existence of associations between groups and features was verified using the chi-square test and the likelihood ratio for race. OA severity was compared between groups using the Kruskal-Wallis test. Quantitative characteristics were described for the groups using summary measures and were compared between groups using Analysis of Variance (ANOVA) for repeated measures followed by Tukey's multiple comparison test. Scores were described according to groups, subgroups and moments of evaluation using summary measures (mean, standard deviation and 95% confidence interval). Values were compared between groups, telephone calls and moments (of assessment) using a three-factor analysis of variance with repeated measures, followed by Tukey's multiple comparison test to compare groups, telephone calls and moments of assessment when needed.

Variations (changes) in the function, pain and quality of life scores were calculated. Changes in the BMI and fat percentage between the two-year follow-up and baseline were also measured. Subsequently, Pearson's correlations were determined between these variations in the scores and between the changes in the scores

and the baseline measures to check for relationships to patient improvement. The variations in scores were described using the qualitative characteristics of the patients and compared between categories using Student's t-test or ANOVA.
The tests were performed with a significance level of 5%. All analyses were carried out using SPSS 17.

RESULTS

Three hundred six patients were assessed for eligibility, and 246 patients met the inclusion criteria; however, only 228 agreed to participate (Figure 1). Twenty-eight patients were assigned to each of the subgroups 2A, 2B, 3A and 3B; 29 patients were assigned to each of the remaining groups. Sixteen patients missed classes (because they lost interest, weather conditions prevented access to the hospital or they could not attend classes when scheduled) and were excluded. At this point, the number of patients in each subgroup varied from 25 (1A, 2B) to 29 (1B, 4B). At the one-year reassessment, four patients had died (one each from subgroups 1A, 1B, 3B and 4A), and 1 patient had undergone total knee replacement (1A). Nine patients quit (lost interest): one from subgroup 1A, one from 2A, one from 3A, two from 4A and four from subgroup 4B (Figure 1). At the two-year reassessment, one patient had died (subgroup 1A), one lost interest and quit (subgroup 3A) and one was not able to attend the evaluation because of family problems (4B). In total, 33 patients were lost from the study, of whom 11 were from subgroup 4, 9 from subgroup 1, 7 from subgroup 3, and 6 from subgroup 2.
Subgroups were homogeneous for nominal valued features, such as degree of KOA, age, gender, race, percentage of body fat, years of schooling, affected side or bilaterality, and questionnaire (subjective) results ($p>0.05$, Tables 1 to 4). The results of WOMAC and the physical and mental components of the SF-36 questionnaires changed timewise but not between subgroups ($p=0.007$, $p=0.020$ and $p=0.027$, respectively). BMI was statistically different between subgroups 2 and 3 ($p=0.047$), but PBF was not ($p=0.464$). The latter varied during the study ($p<0.001$).
The relative proportions of subgroups were maintained when analysing the Class and Control groups with 76.4% and 76.6% women, 62.8% and 68.1% of white race and 68.9% and 72.3% bilaterality, respectively. Both groups had similar percentages of K&L grades II, III and IV (for the Class group: right knee: 33.1%, 37.2% and 20.9%; left knee: 33.3%, 38.8% and 19%, respectively; for the Control group: right knee: 29.5%, 31.8% and 36.4%; left knee: 31.9%, 42.6% and 17%, respectively, $p=0.22$).
Table 5 shows the results of the BMI, PBF, pain and functional questionnaires and functional tests from the Class and Control groups. BMI remained the same timewise in both groups ($p=0.52$ and $p=0.46$, respectively). PBF remained similar in both groups but changed timewise in both groups ($p=0.46$ and $p=0.001$, respectively). The Lequesne questionnaire results were initially similar between groups and later improved in the Class group and worsened in the Control group ($p=0.02$ at two years and $p<0.001$, timewise). TUG and FTSST also showed differences timewise ($p=0.01$ and $p<0.001$, respectively). The intensity of physical activity was similar between groups prior to the program. At the end of the study, the Class group had incorporated more physical activity into their weekly program than the Control group had ($p=0.45$, Table 6).

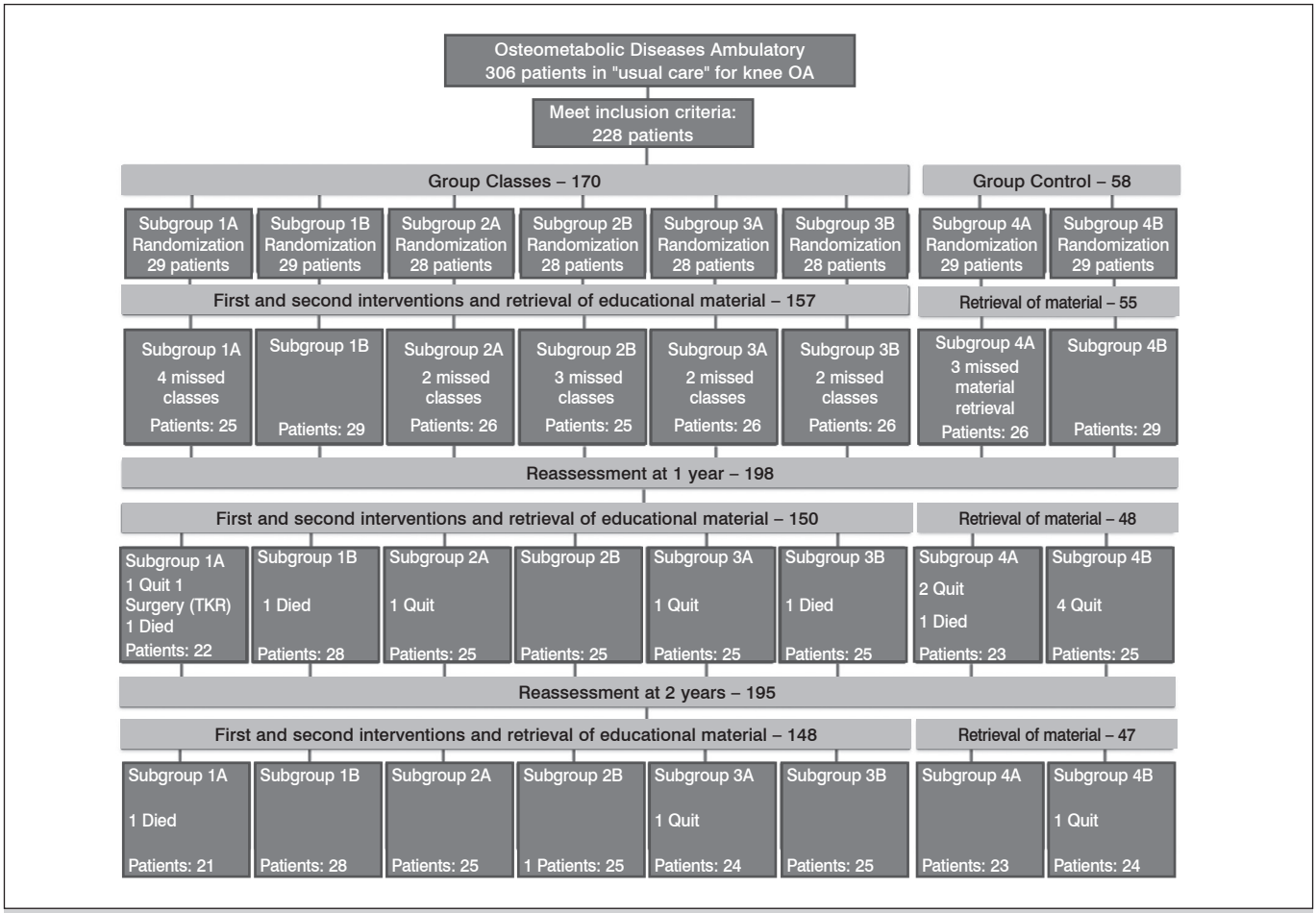

Figure 1. Flow of participants through the trial.

Table 1. Descriptions of personal and clinical characteristics of patients according to the subgroups and results of statistical tests.

	Subgroup								
Variable	**1**		**2**		**3**		**4**		**p**
	n	**%**	**n**	**%**	**n**	**%**	**n**	**%**	
K&L Right									0.149*
0	0	0.0	0	0.0	2	4.1	0	0.0	
1	4	8.2	1	2.0	6	12.2	1	2.3	
2	20	40.8	17	34.0	12	24.5	13	29.5	
3	15	30.6	21	42.0	19	38.8	14	31.8	
4	10	20.4	11	22.0	10	20.4	16	36.4	
K&L Left									0.361*
0	0	0.0	0	0.0	0	0.0	3	6.4	
1	5	10.2	3	6.1	5	10.2	1	2.1	
2	21	42.9	14	28.6	14	28.6	15	31.9	
3	16	32.7	25	51.0	16	32.7	20	42.6	
4	7	14.3	7	14.3	14	28.6	8	17.0	
Gender									0.893
Male	13	26.5	10	20.0	12	24.5	11	23.4	
Female	36	73.5	40	80.0	37	75.5	36	76.6	
Race									0.616#
White	27	56.2	31	63.3	32	66.7	33	70.2	
Mulatto/Mestizo	12	25.0	11	22.4	10	20.8	8	17.0	
Black	9	18.8	5	10.2	5	10.4	4	8.5	
Asian	0	0.0	2	4.1	1	2.1	2	4.3	
Knee									0.745
Right	39	79.6	43	86.0	41	83.7	41	87.2	
Left	10	20.4	7	14.0	8	16.3	6	12.8	
Bilateral									0.866
No	15	30.6	14	28.0	17	34.7	13	27.7	
Yes	34	69.4	36	72.0	32	65.3	34	72.3	

Chi-sqare test; # Likelyhood ratio test; * Kruskal-Wallis's test; K&L: Kellgren and Lawrence.

Table 2. Descriptions of quantitative characteristics according to subgroups and the results of statistical tests.

Variable	Subgroup	Mean	SD	95% CI		n	p
				Lower	Upper		
Age (years)	Subgroup 1	64.4	9.7	61.7	67.1	49	0.108
	Subgroup 2	62.1	8.3	59.8	64.4	50	
	Subgroup 3	66.6	9.8	63.9	69.4	49	
	Subgroup 4	64.3	8.7	61.8	66.8	47	
Time of study (years)	Subgroup 1	7.4	2.7	6.6	8.1	49	0.556
	Subgroup 2	7.8	3.3	6.9	8.7	49	
	Subgroup 3	8.0	3.5	7.0	8.9	49	
	Subgroup 4	8.2	2.2	7.6	8.8	47	
BMI (kg/m^2)	Subgroup 1	31.3	5.2	29.9	32.8	49	0.049
	Subgroup 2	32.8	6.0	31.2	34.5	50	
	Subgroup 3	29.8	4.7	28.5	31.1	49	
	Subgroup 4	31.3	5.2	29.8	32.8	46	
BFP	Subgroup 1	35.8	9.4	33.2	38.4	49	0.421
	Subgroup 2	37.8	7.6	35.7	40.0	50	
	Subgroup 3	35.1	8.2	32.8	37.4	49	
	Subgroup 4	36.3	8.4	33.8	38.7	47	
ANOVA							

SD: Standard Deviation / CI: Confidence Interval / BMI: Body Mass Index / BFP: Body Fat Percentage.

DISCUSSION

Individuals over 60 years of age represented 8.6% of the Brazilian population in 2000 (which was 169,799,170), and the projection for 2030 was 13.44% of all Brazilians (223,126,917).[16,17] The population of the United States in 2010 was 308,745,538, with 13% individuals over 65 years of age. In that same year, in the United States, total knee replacement was the most frequently performed inpatient procedure on adults aged 45 and over.[18] Between 2000 and 2010, an estimated 5.2 million total knee replacements were performed, and adults over 45 years old comprised 98.1% of those surgeries.[19]

Regardless of the low education and socioeconomic status of the Brazilian population, increasing longevity and obesity (74.1% of people over 65 years of Brazil were overweight or obese in 2008-2009) perpetuate the increasing prevalence of OA and a low quality of life.[3-6,20] The aim of this educational program on OA was to teach patients about the nature, causes and treatment of osteoarthritis and, above all, to improve patients' knowledge and health behaviour. The one-year results of the program led to the suspension of bimonthly telephone calls. Telephone calls were time consuming and were not effective in modifying the adherence to the diet program, exercise and social engagement.[7]

Our subgroups and groups were homogeneous as to the degree of KOA (70% grades 2 and 3, and 20% grade 4 K&L), age (average age 64.4 years), gender (approximately 3 women to 1 man), race (60% Caucasians), PBF (approximately 36%), affected side (80% affected the right side) or bilateral (70% with bilateral involvement), and questionnaire results (subjective) ($p>0.05$, Tables 1 and 2). Table 2 shows that subgroups 2 and 3 differed in BMI ($p = 0.049$) but not in PBF ($p = 0.421$). When we consider the Class and Control groups, the groups were similar in all parameters ($p> 0.05$). Tables 3 and 4 show the results of the pain, function and quality of life questionnaires of subgroups 1 to 4 (still registering those who received bimonthly phone calls in the first year of the study). The differences in the results were not significant, as was expected.[7,8]

When comparing the Class and Control groups (Table 5), both groups failed to lose the minimum 6.1 kg for symptomatic improvement (10), but although the Class group improved or maintained functional outcomes in the Lequesne questionnaire, the group that received the educational material only (Control) progressively worsened their Lequesne results ($p=0.02$ between groups, $p<0.001$ over time). Objective tests of TUG and TSL that represent the strength of lower limbs and balance[13,14] improved over time, especially in the Class group.

Both the Class and Control groups were similar with respect to physical activity practiced at baseline (Table 6), but the number of participants who incorporated physical activity and at greater intensity was significantly higher in the group that joined classes ($p=0.045$), thus reinforcing the increased strength and balance observed by the objective TUG and FTSST tests and by the subjective Lequesne questionnaire results.

Our educational program failed to significantly reduce the BMI of the participants (Tables 3-5). Roughly one-third lost weight (at least 1 point in BMI), one-third remained at a similar weight and the last third gained weight. Because obesity and OA yield substantial losses in quality-adjusted life-years,[20] this deficiency in the program needs to be rectified. The project may have raised the awareness of the need for physical activity and diet, but only 12% actually lost more than 2 points in BMI (6.1 kg for a person 1.75 m tall). The increase in physical activity and improved function were the main effects of the educational program.

Table 3. Descriptions of functional (WOMAC and Lequesne) and pain (WOMAC pain) scales according to subgroups and moments.

Subgroup	Calling in the first year		WOMAC			WOMAC Pain			Lequesne		
			Baseline	1 year	2 years	Baseline	1 year	2 years	Baseline	1 year	2 years
1	Yes (A)	Mean (SD)	44 (20.2)	39.1 (15)	35.8 (15.9)	8.8 (4.3)	7.5 (3.3)	7.6 (2.9)	11.2 (4.1)	10.6 (3.4)	10.1 (3.8)
		95% CI	(35.3 - 52.6)	(32.7 - 45.5)	(28.8 – 42.8)	(6.9 - 10.6)	(6.1 - 8.9)	(6.3 - 8.9)	(9.5 - 13)	(9.1 - 12.1)	(8.4 - 11.7)
	No (B)	Mean (SD)	48.8 (15.8)	44.3 (14)	45.3 (16.8)	9.1 (4.3)	8.3 (3.6)	9.4 (3.8)	11.9 (4)	12.4 (3.1)	11.7 (4.7)
		95% CI	(43 - 54.7)	(39.1 - 49.5)	(39.1 – 51.5)	(7.5 - 10.7)	(7 - 9.7)	(8 - 10.8)	(10.4 - 13.4)	(11.3 - 13.6)	(10 - 13.4)
2	Yes (A)	Mean (SD)	49 (17.2)	42 (19.5)	43.2 (21)	9.6 (3.2)	7.7 (3.8)	8.5 (4.6)	12.3 (3.4)	11.6 (4.8)	12.4 (4.7)
		95% CI	(42.2 - 55.7)	(34.4 - 49.6)	(34.8 – 51.6)	(8.4 - 10.9)	(6.2 - 9.2)	(6.7 - 10.4)	(10.9 - 13.6)	(9.7 - 13.5)	(10.5 - 14.3)
	No (B)	Mean (SD)	47.2 (19.3)	44.8 (20.4)	39.4 (16.7)	9.9 (4.4)	8.5 (4.2)	7.8 (3.7)	12.5 (4.3)	11.8 (4.7)	11.4 (3.8)
		95% CI	(39.6 - 54.8)	(36.8 - 52.8)	(32.4 – 46.4)	(8.2 - 11.6)	(6.9 - 10.2)	(6.2 - 9.3)	(10.8 - 14.2)	(9.9 - 13.6)	(9.8 - 13)
3	Yes (A)	Mean (SD)	42.8 (19.5)	43.6 (20)	47.3 (21.2)	8.9 (4)	8.5 (3.9)	9.9 (4.3)	11.6 (4.6)	11.8 (4.5)	12.4 (4.4)
		95% CI	(35 - 50.6)	(35.6 - 51.6)	(38.6 - 56)	(7.3 - 10.5)	(7 - 10.1)	(8.2 - 11.6)	(9.7 - 13.4)	(10 - 13.6)	(10.6 - 14.1)
	No (B)	Mean (SD)	43.8 (19)	42.6 (14.5)	39.4 (16.8)	8.3 (4.3)	8.7 (3.2)	7.3 (3.5)	11.2 (3.8)	12.1 (3.5)	10.9 (4.8)
		95% CI	(36.4 - 51.3)	(36.9 - 48.3)	(32.5 – 46.3)	(6.6 - 10)	(7.5 - 10)	(5.8 - 8.7)	(9.7 - 12.7)	(10.7 - 13.4)	(8.9 - 12.8)
4	Yes (A)	Mean (SD)	44.4 (13.8)	47.5 (19)	45.8 (14.9)	9.4 (4.1)	9.6 (4.7)	9.6 (3.4)	11.9 (4.6)	12.2 (4)	12.6 (4.2)
		95% CI	(38.8 - 50.1)	(39.7 - 55.3)	(39.6 - 52)	(7.7 - 11.1)	(7.7 - 11.5)	(8.1 - 11)	(10 - 13.8)	(10.5 - 13.9)	(10.9 - 14.3)
	No (B)	Mean (SD)	42.6 (21.8)	44.9 (20.1)	42 (15.3)	8 (4.2)	9.1 (3.7)	8.6 (3.2)	12.5 (4.4)	12.3 (4.2)	11.7 (4.2)
		95% CI	(33.9 - 51.3)	(36.8 - 52.9)	(35.4 – 48.5)	(6.4 - 9.7)	(7.6 - 10.6)	(7.2 - 10)	(10.7 - 14.2)	(10.7 - 14)	(9.9 - 13.5)

SD: Standard Deviation / CI: Confidence Interval.

Table 4. Descriptions of pain (VAS) and quality of life (SF-36) scales according to subgroups and moments.

Subgroup	Calling in the first		VAS			SF-36 PCS			SF-36 MCS		
			Baseline	1 year	2 years	Baseline	1 year	2 years	Baseline	1 year	2 years
1	Yes (A)	Mean (SD)	52.3 (25.3)	49.4 (22.2)	48.9 (15.2)	32.3 (8.2)	32.2 (9.1)	36.9 (8.6)	44.4 (12.3)	48.3 (13.1)	49.7 (12.9)
		95% CI	(41.5 - 63.1)	(39.9 - 58.9)	(42.2 - 55.6)	(28.8 - 35.9)	(28.3 - 36)	(33.1 - 40.7)	(39.2 - 49.7)	(42.7 - 53.9)	(44.1 - 55.3)
	No (B)	Mean (SD)	60.6 (24.8)	54.4 (23.2)	53.4 (26.2)	32.6 (8.1)	34.2 (7.3)	34.7 (7.2)	46.6 (14.1)	49.5 (10)	49.2 (13.4)
		95% CI	(51.5 - 69.8)	(45.8 - 63)	(43.6 - 63.1)	(29.6 - 35.6)	(31.5 - 36.9)	(32 - 37.4)	(41.4 - 51.8)	(45.8 - 53.2)	(44.2 - 54.2)
2	Yes (A)	Mean (SD)	67.8 (24.1)	53.4 (23.9)	58.2 (23)	30.3 (6.5)	32 (8.4)	32.5 (6.1)	44 (12.6)	45.8 (14.2)	44.4 (13.6)
		95% CI	(58.3 - 77.2)	(44 - 62.8)	(49 - 67.4)	(27.8 - 32.9)	(28.8 - 35.3)	(30.1 - 35)	(39.1 - 49)	(40.2 - 51.4)	(39 - 49.8)
	No (B)	Mean (SD)	60.8 (28.7)	52.7 (27.5)	53.5 (24.5)	33 (9.1)	33.9 (9.6)	34.4 (7.7)	43.5 (13.1)	47 (13.7)	47.3 (10.6)
		95% CI	(49.6 - 72.1)	(41.9 - 63.4)	(43.3 - 63.7)	(29.4 - 36.5)	(30.2 - 37.7)	(31.2 - 37.7)	(38.4 - 48.7)	(41.6 - 52.4)	(42.9 - 51.7)
3	Yes (A)	Mean (SD)	61.9 (25.2)	56.2 (21)	65.8 (19)	31.9 (9)	33.1 (7.9)	31.8 (9.3)	48.9 (11.2)	49 (11)	44 (12.7)
		95% CI	(51.8 - 72)	(47.8 - 64.6)	(58 - 73.5)	(28.3 - 35.5)	(30 - 36.3)	(27.9 - 35.6)	(44.4 - 53.4)	(44.6 - 53.3)	(38.8 - 49.2)
	No (B)	Mean (SD)	46.8 (28.3)	53.7 (24.1)	51.5 (13.8)	34.7 (7.7)	36.1 (10.3)	37.7 (9.2)	46.8 (9.9)	49.7 (10)	49.7 (9.1)
		95% CI	(35.7 - 57.8)	(44.2 - 63.1)	(45.9 - 57.1)	(31.7 - 37.7)	(32.1 - 40.2)	(33.9 - 41.5)	(42.9 - 50.6)	(45.7 - 53.6)	(45.9 - 53.4)
4	Yes (A)	Mean (SD)	53 (25.8)	59.8 (26.7)	63.5 (18)	33.6 (7.7)	32.7 (8.1)	32.8 (7.3)	45.4 (12.1)	48.6 (17)	45.5 (11.1)
		95% CI	(42.4 - 63.5)	(48.9 - 70.7)	(55.9 - 71)	(30.4 - 36.7)	(29.4 - 36)	(29.8 - 35.9)	(40.5 - 50.4)	(41.7 - 55.6)	(40.9 - 50.2)
	No (B)	Mean (SD)	61.7 (28.7)	62 (21.5)	61.2 (19.2)	33.7 (7.5)	34.6 (8.6)	34.5 (8.1)	43.3 (13.3)	43.6 (13.9)	41.4 (13.1)
		95% CI	(50.2 - 73.1)	(53.4 - 70.6)	(53 - 69.4)	(30.7 - 36.7)	(31.2 - 38)	(31.1 - 38)	(38 - 48.7)	(38 - 49.1)	(35.7 - 47)

SD: Standard Deviation / CI: Confidence Interval / VAS: Visual Analog Scale; SF-36 PCS: Medical Outcomes Study - 36 Itens Short Form Health Survey - Physical Component Summary; SF-36 MCS: Medical Outcomes Study - 36 Itens Short Form Health Survey - Mental Component Summary.

Table 5. Descriptions of anthropometric measures, pain and functional scales and functional tests (TUG and FTSST) according to subgroups and moments.

		Group Class			Group Control			Significance	
		Baseline	1 year	2 years	Baseline	1 year	2 years	Between Groups	Time
								p	p
BMI	Mean (SD)	31.29 (5.41)	31.14 (5.37)	31.44 (5.33)	31.30 (5.19)	31.15 (5.79)	31.44 (6.18)	0.52	0.46
	CI	30.14 - 32.37	30.11 - 32.30	30.26 - 32.35	29.48 - 33.96	29.00 - 34.04	28.51 - 33.64		
BFP	Mean (SD)	36.26 (8.46)	35.75 (8.56)	38.34 (8.39)	36.26 (8.45)	35.96 (8.11)	37.73 (8.49)	0.46	0.001*
	CI	34.32 - 37.87	33.94 - 37.56	36.37 - 40.06	33.92 - 41.05	33.80 - 40.68	33.40 - 42.64		
Womac	Mean (SD)	46.07 - (18.31)	42.85 (17.22)	42.01 (18.32)	43.51 (18.14)	46.15 (19.42)	43.91 (15.02)	0.74	0.47
	CI	40.42 - 48.80	38.85 - 46.27	35.57 - 43.26	36.61 - 48.49	34.05 - 50.85	34.62 - 48.18		
Womac Pain	Mean (SD)	9.11 (4.06)	8.23 (3.67)	8.47 (3.91)	8.00 (4.12)	9.00 (4.17)	9.00 (3.33)	0.40	0.68
	CI	8.09 - 9.88	7.44 - 9.04	7.15 - 8.77	7.32 - 10.68	6.81 - 9.99	6.56 - 9.74		
VAS	Mean (SD)	58.55 (26.58)	53.39 (23.47)	55.31 (21.42)	57.4 (27.36)	60.89 (23.96)	62.35 (18.45)	0.14	0.88
	CI	51.44 - 62.75	47.01 - 56.98	46.27 - 55.20	45.84 - 69.76	41.05 - 65.45	50.32 - 68.28		
Lequesne	Mean (SD)	11.81 (4.09)	11.76 (4.02)	11.51 (4.39)	11.97 (3.71)	12.26 (4.06)	12.16 (4.13)	0.02	<0.001*
	CI	10.61 - 12.48	10.46 - 12.18	9.81 - 11.72	9.61 - 13.34	9.98 - 13.37	9.45 - 13.25		
Time-Up-and-Go	Mean (SD)	12.2 (4.42)	12.08 (4.37)	11.79 (4.87)	13.71 (6.00)	12.6 (4.73)	12.6 (5.20)	0.31	0.01*
	CI	11.11 - 13.23	10.95 - 12.83	10.29 - 12.09	11.63 - 16.40	10.92 - 15.66	9.89 - 15.15		
Five-Times-Sit-to-Stand	Mean (SD)	23.23 (8.26)	18.17 (5.96)	19.43 (6.65)	22.79 (11.08)	19.66 (10.26)	23.24 (10.49)	0.13	<0.001*
	CI	21.26 - 25.13	16.71 - 19.13	18.13 - 20.84	18.10 - 29.69	15.42 - 26.53	18.08 - 29.76		

SD: Standard Deviation; CI: Confidence Interval; BMI: Body Mass Index; BFP: Body Fat Percentage; VAS: Visual Analog Scale.

Table 6. Description of the intensity of physical activity weekly practiced according to subgroups and moments of evaluation and results of the comparative tests.

	Baseline				2 years			
	Group Class		Group Control		Group Class		Group Control	
Intensity of physical activity	n	%	n	%	n	%	n	%
Does not perform	118	84.9%	40	90.9%	38	27.3%	22	50.0%
Light activity	7	5.0%	4	9.1%	60	43.2%	14	31.8%
Moderate activity	12	8.6%	0	0.0%	33	23.7%	7	15.9%
Vigorous activity	2	1.4%	0	0.0%	8	5.8%	1	2.3%
	p = 0.139				p = 0.045			

Chi-squared test.

CONCLUSION

The educational program with classes improved the performance of physical activity and both subjective and objective function of patients with KOA.

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INTENSITY, DURATION AND TYPE OF PHYSICAL ACTIVITY REQUIRED TO IMPROVE FUNCTION IN KNEE OSTEOARTHRITIS

INTENSIDADE, DURAÇÃO E TIPO DE ATIVIDADE FÍSICA PARA MELHORA DA FUNÇÃO NA GONARTRITE

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ABSTRACT

Objective: To evaluate the effects of physical activity intensity, type and duration in patients with knee osteoarthritis (KOA). Methods: A retrospective study of 195 KOA patients who were followed for two years after receiving educational material about KOA with or without attending classes. The patients were evaluated at baseline and 24 months. At the evaluations, the patients answered questionnaires pertaining to pain and function (WOMAC, Lequesne, VAS and SF-36); reported the intensity, duration and type of exercise performed per week; and performed the Timed Up & Go (TUG) and Five Times Sit-to-Stand (FTSST) tests. Results: Increased age affected improvements in the TUG results ($p=0.017$). The type, intensity and duration of physical activity did not correlate with pain, function or quality of life improvements ($p>0.05$), but the TUG results were on average 4 seconds faster among the patients who practiced intense physical activity and/or exercised for more than 180 minutes per week and/or performed isolated weight training or swam compared with those who remained sedentary after 2 years ($p=0.01$; $p<0.001$; $p=0.01$; $p=0.04$, respectively). Conclusions: Patients with KOA should aim for intense physical activity and/or more than 180 minutes of exercise per week and/or weight training (bodybuilding) for relevant pain reduction and functional improvement. ***Level of Evidence II, Retrospective Study.***

Keywords: Osteoarthritis. Knee. Patient education as topic. Motor activity. Treatment outcome.

RESUMO

Objetivo: Avaliar o efeito da intensidade, tipo e tempo da atividade física semanal em pacientes com osteoartrite do joelho (OAJ). Métodos: Cento e noventa e cinco pacientes portadores de OAJ foram acompanhados por dois anos após receberam material educacional sobre OAJ, com ou sem aulas. Os pacientes responderam aos questionários de dor, função, qualidade de vida (WOMAC, Lequesne, EVA e SF-36), intensidade, frequência e tipo de atividade física semanal realizada, além de realizaram os testes de senta e levanta (TSL) e "Timed-Up-and-Go" (TUG) no momento da inclusão e após 24 meses. Resultados: O aumento da idade dos pacientes acarretou menor chance de melhora no TUG ($p=0,017$). O tipo de atividade física, intensidade e frequência não mostraram correlação com melhoras algo-funcionais e de qualidade de vida ($p>0,05$), porém os resultados do TUG foram em média 4 seg mais rápidos em pacientes que praticavam atividade física intensa e/ou acima de 180 min por semana e/ou musculação isolada, ou ainda, musculação ou natação, em relação aos pacientes sedentários ($p=0,01$; $p<0,001$; $p=0,01$; $p=0,04$, respectivamente) após dois anos. Pacientes praticantes de musculação tinham menos dor que os sedentários após o programa ($p=0,009$). Conclusão: Pacientes com OAJ são aconselhados a objetivar atividade física intensa e/ou acima de 180 min por semana e/ou musculação para atingir melhora algo-funcional relevante. ***Nível de Evidência II, Estudo Retrospectivo.***

Descritores: *Osteoartrite. Joelho. Educação de pacientes como assunto. Atividade motora. Resultado do tratamento.*

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INTRODUCTION

Osteoarthritis is the leading cause of disability among chronic diseases.[1-3] The societal and personal costs of functional limitation resulting from osteoarthritis are high among older adults.[4,5] Medical expenses among the elderly are more closely related to functional losses than to life expectancy.[6,7]

A lack of regular vigorous physical activity is a potentially modifiable risk factor that could substantially reduce functional decline and related health care costs. Prevention/intervention programs should include regular vigorous physical activity, weight maintenance, and medical intervention for health needs.[8]

We developed an educational program for patients with knee osteoarthritis (KOA) that led to functional improvement and increased adherence to regular physical activity.[9,10] However, the intensity, duration and type of physical activity that is necessary to produce significant functional gains is still unknown. Based on this need, we searched for a correlation between pain, functional and quality of life improvements and absolute results and the intensity, duration

All the authors declare that there is no potential conflict of interest referring to this article.

Study conducted at Universidade de São Paulo, Faculdade de Medicina, Department of Orthopedics and Traumatology, Laboratório de Investigação Médica do Sistema Musculoesquelético, Osteometabolic Diseases Group, São Paulo, SP, Brazil.
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and type of physical activity practiced by patients to determine a physical activity goal that would allow patients with KOA to obtain clinically relevant functional improvements.

METHODS

This study was performed at the Department of Orthopedics and Traumatology, São Paulo, Brazil, after it was approved by the Ethics Committee for the Analysis of Research Projects (CAPPesq) under protocol number 0622/11.

Clinical trials registration number: NCT01572051.

One hundred ninety-five patients with KOA (46 men, 149 women, age 68 ± 9.2 years and BMI 31.1 ± 5.4 at inclusion) who participated in a two-year educational program for patients with KOA at the Osteometabolic Diseases Group Department of Orthopedics, Hospital das Clínicas, University of São Paulo participated in this study.

The patients had to meet the following criteria: outpatients who were aged 45 years or older with KOA diagnosed according to the American College of Rheumatology clinical and radiological definition,[11] had no rheumatoid arthritis or rheumatologic disease other than OA, had been receiving clinical treatment for OA in the past thirty months and had participated in the PARQVE educational program for patients with OAJ.[9,10] The exclusion criteria were 1) KOA surgery during the study period or other surgery during the study period that would prevent regular physical activity, and 2) participation in another nutritional education program or another clinical study. Patients who were not able to perform or did not attend the functional tests were excluded only from the functional analysis.

Intervention

At enrollment and 24 months later, the patients were asked to respond to VAS (visual analog pain scale), WOMAC™, Lequesne, and SF-36 questionnaires and to report the duration, intensity and type of physical activity they performed each week.[12-15] The patients were asked to perform the timed up-and-go (TUG) test and the five times sit-to-stand (FTSST) test.[16-18]

All of the participants received information on OA disease and its treatment in the form of classes and/or educational materials that included the class content in text and video (DVD) form.[9,10] The DVD was 2 hours and 23 minutes long. All of the patients were instructed to watch the DVD and/or read the handout at least three times and to exercise under the guidance of physical therapists or physical educators (via information of the handout or at public or private gyms) at least three times a week.

Statistical analysis

Improvement criteria were established for each of the scores and functionality testing: a reduction of at least 10 points on the total WOMAC score, 4 points on the WOMAC pain score, 2 points on the WOMAC stiffness score, 5 points on the WOMAC physical function score, 4 seconds on the TUG and 4 seconds on the TSL.

The quantitative characteristics were described as improvement for each criterion with the use of summary measures (mean, standard deviation, median, minimum and maximum) and were compared using Student's t or Mann-Whitney tests. Improvements in each criterion were described according to their qualitative characteristics and association using likelihood ratios or chi-square tests.

Odds ratios (ORs) were estimated for the association between each variable of interest and improvement in each criterion along with the respective 95% confidence intervals, based on simple logistic regression.

Multiple saturated logistic regression models were estimated for each of the improvement criteria.

The tests were performed at the 5% significance level.

RESULTS

There was no relationship between improvement in the WOMAC, VAS, Lequesne, SF-36, TUG and FTSST scores and the type, intensity and duration of physical activity (all $p > 0.05$).

Table 1 shows that increasing age was associated with a lower likelihood of improvement in the TUG score, regardless of the other characteristics evaluated. With each additional year of age, there was a 7% reduction in the chance of improvement on the TUG test, OR = 0.93, p = 0.017.

When comparing patients who engaged in intense physical activity with those who did not engage in any physical activity, we found that at enrollment, the few (three) patients who practiced intense physical activity had less pain than the 157 sedentary patients ($p=0.02$). After two years of participating in the PARQVE[9,10] program, the 19 patients who practiced intense physical activity completed the TUG an average of 4 seconds faster than the sedentary group ($p = 0.01$, Table 2) and reported less pain (50.9±15.3) than those who did not engage in any physical activity (59.4±23.1) but not significantly (Table 2).

After two years of the program, the 46 patients who exercised 180 minutes or more per week also completed the TUG an average of 4 seconds faster than the 56 sedentary patients ($p<0.001$, Table 3).

The participants who performed regular physical activity engaged in a wide variety of activities (exercises provided in the program handout, water aerobics, yoga, walking, weight training, swimming, stretching, tai chi chuan, bike riding, Pilates). Bodybuilders reported less pain ($p = 0.009$) and performed the TUG approximately 4 seconds faster than sedentary patients ($p = 0.01$, Table 4). The addition of the results for those who swam to the body builders' results maintained the difference from sedentary patients in terms of pain ($p = 0.03$) and TUG times (0.04, Table 5).

DISCUSSION

As the most common form of joint disease, osteoarthritis (OA) is associated with an extremely high economic burden. This burden is largely attributable to the effects of disability, comorbid disease, and the expense of treatment.[19]

Among a cohort of 5,715 adults aged 65 years or older with arthritis, a lack of regular vigorous physical activity was the most prevalent risk factor (64%); it almost doubled the odds of functional decline (adjusted OR 1.9, 95% confidence interval 1.5–2.4) after controlling for all risk factors. If all subjects engaged in regular vigorous physical activity, the expected functional decline could be reduced by as much as 32%.[8]

In our series, we could not show any relation between improved pain, function or quality of life scores and the intensity, duration or type of physical activity (all $p>0.05$). This lack of association may be explained by the relatively small number of patients who engaged in intense physical activity (20) and by the fact that although many of our patients reported that they performed the exercises provided in the educational booklet on a regular basis, they did not actually do all of them (several chose to perform only the stretching exercises, and those who did perform the strength exercises did not regularly increase the load). However, age emerged as a barrier to improving inferior limb strength, function and balance, as determined by TUG performance[16,17]; this finding is consistent with those of Dunlop et al.[8]

The patients who already practiced intense physical activity at the time of enrollment reported less pain than those that were sedentary (Table 2). This finding is supported by a meta-analysis of 54 eligible trials (20 pharmacology, 34 exercise), including six Cochrane reviews (four pharmacology, two exercise,) with 9806 participants (5627 pharmacology, 4179 exercise). This meta-analysis reported a pooled effect size for pharmacological pain interventions of 0.41 (95% CI: 0.23-0.59); for exercise, the pooled effect size was 0.46 standardized mean difference (95% CI: 0.34-0.59). This

Table 1. Description of quantitative characteristics according to improvements in the TUG time, qualitative characteristics and statistical test results.

Variable	Improves TUG		Total	OR	IC (95%)		p	OR	IC (95%)		p
	No	Yes		unadjusted	Lower	Upper		adjusted	Lower	Upper	
Type of physical activity, n (%)							0,561				
Sedentary	40 (85.1)	7 (14.9)	47	1.00				1.00			
Booklet/Stretching	26 (76.5)	8 (23.5)	34	1.76	0.57	5.43		#			0.999
Walking/Fitness/Water Aerobics	51 (87.9)	7 (12.1)	58	0.78	0.25	2.42		#			0.999
Swimming/Bicycle/Bodybuilding	17 (85)	3 (15)	20	1.01	0.23	4.37		#			0.999
Intensity of physical activity, n (%)							0.829				
Sedentary	44 (88)	6 (12)	50	1.00				1.00			
Light	54 (83.1)	11 (16.9)	65	1.49	0.51	4.36		#			0.999
Moderate	29 (85.3)	5 (14.7)	34	1.26	0.35	4.53		#			0.999
Vigorous	7 (77.8)	2 (22.2)	9	2.10	0.35	12.53		#			0.999
Minutes per Week				0.999	0.995	1.002	0.598*	0.995	0.988	1.002	0.176
Mean (SD)	124.7 (136.9)	101.7 (105.6)	121.2 (132.6)								
Median (min.; max.)	100 (0; 840)	70 (0; 390)	95 (0; 840)								
Age (years)				0.96	0.92	1.01	0.144	0.93	0.87	0.99	0.017
Mean (SD)	67.6 (8.5)	64.8 (10)	67.2 (8.8)								
Median (min.; max.)	68 (48; 87)	65 (47; 84)	67 (47; 87)								
Gender, n (%)							0.194*				
Male	32 (91.4)	3 (8.6)	35	1.00				1.00			
Female	103 (82.4)	22 (17.6)	125	2.28	0.64	8.11		4.89	0.55	43.66	0.155
Race, n (%)							0.536				
White	86 (83.5)	17 (16.5)	103	1.00				1.00			
Mulatto/Mestizzo	26 (81.2)	6 (18.8)	32	1.17	0.42	3.27		0.70	0.20	2.52	0.587
Black	18 (90)	2 (10)	20	0.56	0.12	2.65		0.35	0.06	2.02	0.24
Asian	4 (100)	0 (0)	4	#				#			0.999
Bilateral, n (%)							0.165*				
No	46 (90.2)	5 (9.8)	51	1.00				1.00			
Yes	89 (81.7)	20 (18.3)	109	2.07	0.73	5.86		2.36	0.71	7.87	0.163
BMI				1.04	0.96	1.13	0.356	0.98	0.87	1.12	0.799
Mean (SD)	31.2 (5.3)	32.3 (5.1)	31.4 (5.2)								
Median (min.; max.)	30.7 (19.8; 49.9)	31.2 (25.9; 45.8)	30.8 (19.8; 49.9)								
BFP				1.02	0.97	1.08	0.409	1.00	0.89	1.14	0.961
Mean (SD)	38.1 (8.4)	39.6 (7.7)	38.3 (8.3)								
Median (min.; max.)	40.4 (10.1; 49.1)	40.7 (18.5; 48)	40.4 (10.1; 49.1)								
Study time				0.99	0.86	1.14	0.721*	0.96	0.82	1.13	0.6
Mean (SD)	8 (3.1)	7.9 (3)	8 (3)								
Median (min.; max.)	8 (1; 15)	8 (1; 15)	8 (1; 15)								

The total number of cases varies by variable; Interaction between the type of activity and intensity (p> 0.999); Quantitative variables: Student's t test; * Mann-Whitney test; qualitative variables: the likelihood ratio test; * Chi-square test.

Table 2. Description of the test and scale results at baseline and after 2 years for patients who did not engage in regular physical activity and patients who engaged in intense regular physical activity and the results of comparative tests.

Variable		Baseline				p		2 years				p
		n	Sedentary	n	Vigorous activity			n	Sedentary	n	Vigorous activity	
WOMAC pain												
Mean (SD)		157	8.9 (4.2)	3	5 (1.7)	0.10		56	8.7 (3.9)	20	7.4 (3.4)	0.28
Median (min.; max.)			9 (0 - 20)		4 (4 - 7)				8 (1 - 17)		7 (2 - 15)	
WOMAC stiffness												
Mean (SD)		157	3.4 (1.9)	3	2.3 (1.2)	0.31		56	3.2 (2.1)	20	2.9 (2.0)	0.60
Median (min.; max.)			3 (0 - 8)		3 (1 - 3)				3 (0 - 8)		3 (0 - 6)	
WOMAC function limitation												
Mean (SD)		157	31.7 (12.4)	3	20.7 (8.1)	0.10		56	31 (14.0)	20	26.6 (12.8)	0.24
Median (min.; max.)			32 (4 - 63)		16 (16 - 30)				32 (2 - 65)		27.5 (2 - 46)	
WOMAC total												
Mean (SD)		157	44.5 (18.2)	3	28.7 (6.4)	0.10		56	42.8 (19.1)	20	36.8 (17.4)	0.26
Median (min.; max.)			45 (5 - 87)		26 (24 - 36)				42 (0 - 84)		36 (6 - 64)	
VAS												
Mean (SD)		157	58.1 (26.4)	3	23 (3.5)	0.02*		56	59.4 (23.1)	20	50.9 (15.3)	0.08
Median (min.; max.)			60 (2 - 100)		25 (19 - 25)				60 (5 - 100)		51.5 (20 - 80)	
Lequesne												
Mean (SD)		157	11.6 (4.2)	3	8.3 (2.1)	0.10		56	12.1 (4.9)	20	10.7 (3.8)	0.09
Median (min.; max.)			12 (1.5 - 24)		9 (6 - 10)				12.3 (0 - 21)		10.8 (2.5 - 18.5)	
SF 36 - PCS												
Mean (SD)		157	32.8 (8.2)	3	38.8 (4.3)	0.13		56	34.4 (9.2)	20	35.4 (7.6)	0.67
Median (min.; max.)			32.1 (14.3 - 58.1)		21.2 (33.8 - 41.4)				34.4 (15.5 - 57.2)		33.1 (24.4 - 53.8)	
SF 36 - MCS												
Mean (SD)		157	45.6 (12.6)	3	53.0 (8.6)	0.26		56	45 (13.2)	20	47.0 (11.8)	0.55
Median (min.; max.)			44.5 (17.1 - 71.6)		51.2 (45.5 - 62.4)				44.5 (17.3 - 68.7)		43.7 (30.7 - 66.8)	
Timed Up and Go												
Mean (SD)		149	12.3 (4.0)	2	15.5 (11.7)	0.99		52	14.6 (11.6)	19	9.7 (2.1)	0.01*
Median (min.; max.)			11.2 (5.2 - 28.6)		15.5 (7.2 - 23.7)				11.3 (7.0 - 84.6)		9.4 (6.2 - 14.6)	
Five times sit to stand												
Mean (SD)		140	23 (8.2)	2	15.6 (5.7)	0.14		49	22.1 (12.1)	19	18.6 (5.0)	0.34
Median (min.; max.)			22 (11.1 - 66.4)		15.6 (11.6 - 19.6)				20.8 (10.5 - 81.6)		18.0 (10.5 - 27.8)	

Table 3. Description of the 2-year scale and test results for patients who did not engage in regular physical activity and patients who exercised 180 minutes or more/week and the results of comparative tests.

Variable	Time of physical activity per week				p
	n	Sedentary	n	≥180 min. exercise	
WOMAC pain					
Mean (SD)	60	8.7 (3.7)	48	7.8 (3.4)	0.28
Median (min.; max.)		8 (1 - 17)		2 (2 - 15)	
WOMAC stiffness					
Mean (SD)	60	3.4 (2.1)	48	3.4 (1.8)	0.79
Median (min.; max.)		3 (0 - 8)		4 (0 - 6)	
WOMAC function limitation	60		48		0.35
Mean (SD)		30.9 (14.0)		28.0 (12.9)	
Median (min.; max.)		32 (2 - 65)		30 (2 - 51)	
WOMAC total					
Mean (SD)	60	42.6 (18.4)	48	38.9 (17.3)	0.38
Median (min.; max.)		42 (0 - 84)		41 (6 - 70)	
VAS					
Mean (SD)	60	59.2 (22.7)	48	52.5 (21.8)	0.12
Median (min.; max.)		60 (5 - 100)		58 (0 - 94)	
Lequesne					
Mean (SD)	60	12.0 (4.9)	48	10.4 (4.2)	0.08
Median (min.; max.)		12.3 (0 - 21)		11 (2 - 18.5)	
SF 36 - PCS					
Mean (SD)	60	34.1 (8.9)	48	36 (8)	0.18
Median (min.; max.)		34.1 (17 - 57.2)		36.8 (19.6 - 53.8)	
SF 36 - MCS					
Mean (SD)	60	45.2 (13.0)	48	48.3 (11.6)	0.20
Median (min.; max.)		44.5 (17.3 - 68.7)		48.8 (20.8 - 66.8)	
Timed Up and Go					
Mean (SD)	56	14.6 (11.2)	46	10.1 (3.3)	<0.001*
Median (min.; max.)		11.3 (7.0 - 84.6)		9.2 (6.2 - 24.9)	
Five times sit to stand					
Mean (SD)	53	22 (11.8)	45	20.5 (8.5)	0.46
Median (min.; max.)		20.1 (10.5 - 81.6)		18.1 (12.3 - 51.5)	

meta-analysis provided indirect evidence that for KOA pain, the effects of exercise and those of oral analgesics are comparable.[20] After two years, the group that engaged in intense physical activity performed the TUG test faster (9.7±2.1 seconds) than those who remained sedentary (14.6±11.6 seconds, p=0.01, Table 2), in accordance with the expected effect of intense physical activity described above.[8] Not all patients are able to engage in intense physical activity (in our series, only 20 did so; some but not all of the other patients were capable of engaging in intense physical activity); in such cases, the weekly duration and type of physical activity may compensate for a decrease in intensity. Forty-six subjects engaged in regular physical activity for 180 minutes per week or more; on average, those patients performed the TUG test 4 seconds faster than the 56 patients who remained sedentary (p<0.001, Table 3). Regular exercise for 180 minutes or more per week may become goal or a means to performing intense physical activity in the future among patients with KOA.

The large variety of physical activity types was definitely responsible for the lack of significant correlations. The participants who participated in bodybuilding (weight training at the gym) and swimming, activities closely related to greater exercise intensity, reported less pain (p=0.009 and p=0.04, respectively) and faster TUG performances compared with the sedentary participants (p=0.001 and p=0.03, respectively, Tables 4 and 5).

Our study has limitations. It is a retrospective cohort study in which few participants engaged in regular intense physical activity and with considerable variety in the types of physical activities that the participants reported. Both, diversity of physical activity and number of participants actually engaging intense physical activity, diminished the power of the test for the N and demand prospective studies for this question. Among the study's strengths, it provides directions for future prospective randomized studies, such as carefully selecting the included age groups and restricting the types, duration and intensity of physical activity.

Table 4. Description of the 2-year scale and test results for patients who did not engage in regular physical activity and patients who swam or participated in bodybuilding and the results of comparative tests.

Variable		n	Sedentary	n	Swimming	p		n	Sedentary	n	Bodybuilding	p
WOMAC pain	Swimming						Bodybuilding					
Mean (SD)		56	8.7 (3.9)	7	7.4 (1.9)	0.37		56	8.7 (3.9)	12	6.4 (4.1)	0.1
Median (min.; max.)			8 (1 - 17)		6 (6 - 11)				8 (1 - 17)		7 (2 - 15)	
WOMAC stiffness												
Mean (SD)		56	3.2 (2.1)	7	3.1 (1.7)	0.98		56	3.2 (2.1)	12	2.6 (2.2)	0.4
Median (min.; max.)			3 (0 - 8)		4 (0 - 5)				3 (0 - 8)		2.5 (0 - 6)	
WOMAC function limitation						0.63						0.1
Mean (SD)		56	31 (14.0)	7	29.2 (5.3)			56	31 (14.0)	12	23.3 (14.6)	
Median (min.; max.)			32 (2 - 65)		27 (22 - 37)				32 (2 - 65)		25.5 (2 - 45)	
WOMAC total												
Mean (SD)		56	42.8 (19.1)	7	40.1 (7)	0.70		56	42.8 (19.1)	12	32.4 (19.6)	0.12
Median (min.; max.)			42 (0 - 84)		36 (34 - 52)				42 (0 - 84)		36 (6 - 64)	
VAS												
Mean (SD)		56	59.4 (23.1)	7	59.6 (16.5)	0.84		56	59.4 (23.1)	12	42.6 (18.5)	0.009*
Median (min.; max.)			60 (5 - 100)		59 (44 - 93)				60 (5 - 100)		43 (12 - 75)	
Lequesne												
Mean (SD)		56	12.1 (4.9)	7	11.6 (2.0)	0.69		56	12.1 (4.9)	12	9.2 (4.5)	0.06
Median (min.; max.)			12.3 (0 - 21)		11.5 (9 - 14)				12.3 (0 - 21)		9 (2.5 - 18.5)	
SF 36 - PCS												
Mean (SD)		56	34.4 (9.2)	7	34.4 (6.4)	1		56	34.4 (9.2)	12	37.4 (8.3)	0.26
Median (min.; max.)			34.4 (15.5 - 57.2)		31.9 (28 - 43.7)				34.4 (15.5 - 57.2)		39.4 (24.4 - 53.8)	
SF 36 - MCS												
Mean (SD)		56	45 (13.2)	7	41.0 (5.8)	0.45		56	45 (13.2)	12	51.1 (11.6)	0.13
Median (min.; max.)			44.5 (17.3 - 68.7)		42.5 (33 - 47.2)				44.5 (17.3 - 68.7)		50.4 (32 - 66.8)	
Timed Up and Go												
Mean (SD)		52	14.6 (11.6)	7	11.7 (3.1)	0.86		52	14.6 (11.6)	11	9.4 (2.8)	0.01*
Median (min.; max.)			11.3 (7.0 - 84.6)		11.3 (8.5 - 17.9)				11.3 (7.0 - 84.6)		9.2 (6.2 - 14.6)	
Five times sit to stand												
Mean (SD)		49	22.1 (12.1)	7	22.1 (5.9)	0.37		49	22.1 (12.1)	11	17.7 (5.3)	0.14
Median (min.; max.)			20.8 (10.5 - 81.6)		22.9 (14.9 - 30)				20.8 (10.5 - 81.6)		15.4 (10.5 - 27.8)	

Table 5. Description of the 2-year scale and test results for patients who did not engage in regular physical activity and patients who swam or participated in bodybuilding and the results of comparative tests.

Variable	n	Sedentary	n	Bodybuilding or swimming	p
WOMAC pain					
Mean (SD)	56	8.7 (3.9)	19	6.9 (3.5)	0.12
Median (min.; max.)		8 (1 - 17)		7 (2 - 15)	
WOMAC stiffness					
Mean (SD)	56	3.2 (2.1)	19	2.8 (2.0)	0.54
Median (min.; max.)		3 (0 - 8)		3 (0 - 6)	
WOMAC function limitation					
Mean (SD)	56	31 (14.0)	19	25.5 (12.2)	0.13
Median (min.; max.)		32 (2 - 65)		27.5 (2 - 45)	
WOMAC total					
Mean (SD)	56	42.8 (19.1)	19	35.3 (16.3)	0.16
Median (min.; max.)		42 (0 - 84)		36 (6 - 64)	
VAS					
Mean (SD)	56	59.4 (23.1)	19	48.9 (19.2)	0.03*
Median (min.; max.)		60 (5 - 100)		45 (12 - 93)	
Lequesne					
Mean (SD)	56	12.1 (4.9)	19	10 (3.9)	0.10
Median (min.; max.)		12.3 (0 - 21)		11 (2.5 - 18.5)	
SF 36 - PCS					
Mean (SD)	56	34.4 (9.2)	19	36.3 (7.6)	0.39
Median (min.; max.)		34.4 (15.5 - 57.2)		38.2 (24.4 - 53.8)	
SF 36 - MCS					
Mean (SD)	56	45 (13.2)	19	47.4 (10.9)	0.47
Median (min.; max.)		44.5 (17.3 - 68.7)		44.4 (32 - 66.8)	
Timed Up and Go					
Mean (SD)	52	14.6 (11.6)	18	10.3 (3.1)	0.04*
Median (min.; max.)		11.3 (7.0 - 84.6)		9.6 (6.16 - 17.9)	
Five times sit to stand					
Mean (SD)	49	22.1 (12.1)	18	19.4 (5.8)	0.57
Median (min.; max.)		20.8 (10.5 - 81.6)		17.7 (10.5 - 30)	

CONCLUSION

Patients with KOA should aim for intense physical activity and/or more than 180 minutes of exercise per week and/or weight training (bodybuilding) for relevant pain reduction and functional improvement.

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ORIGINAL ARTICLE

COMPARISON BETWEEN RENDERING 3D-CT AND TRANSPARENT 3D-CT IN ACL TUNNEL POSITIONING

COMPARAÇÃO ENTRE 3D-TC POR RENDERIZAÇÃO E 3D-TC POR TRANSPARÊNCIA NO POSICIONAMENTO DE TÚNEIS DO LCA

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ABSTRACT

Objective: To compare the transparent 3D computed tomography (CT) image protocol against conventional 3D-CT image-rendering protocol to assess femoral tunnel position in anatomic anterior cruciate ligament (ACL) reconstructions. Methods: Eight knee CT scans from cadavers were analyzed by image rendering 3D-CT protocol, using Rhinoceros® software. The central point of the ACL tunnel was set using the sagittal plane. Same CT scans were analyzed using transparent 3D-CT measurement protocol with OsiriX® software. Central point of the ACL tunnel was set using sagittal, coronal and axial planes. The grid system described by Bernard and Hertel was used to compare tunnel positions between protocols, using height and length parameters. Results: There was a significant difference between measurements using image rendering 3D-CT and transparent 3D-CT protocol for height (23.8 ± 7.9mm and 33.0 ± 5.0mm, respectively; p=0.017) and no differences for length (18.6 ± 4.2mm and 18.3 ± 4.5mm, respectively; p=0.560). Conclusion: Height in transparent CT protocol was different and length was the same as compared to 3D-CT rendering protocol in Bernard and Hertel method for tunnel measurements. ***Level of Evidence II, Descriptive Laboratory Study.***

Keywords: Anterior cruciate ligament reconstruction. Imaging, Three-Dimensional. Image processing, computer-assisted.

RESUMO

Objetivo: Comparar o protocolo de tomografia computadorizada (TC) 3D por transparência com o protocolo TC-3D por renderização de imagem na avaliação do posicionamento de túneis femorais na reconstrução anatômica do ligamento cruzado anterior (LCA). Método: Oito TC de joelho de cadáveres foram analisadas pelo protocolo de renderização de imagem 3D-TC utilizando o software Rhinoceros®. O ponto central do túnel do LCA foi definido pelo plano sagital. As mesmas tomografias foram analisadas pelo protocolo 3D-TC por transparência, com o software OsiriX®. O ponto central do túnel do LCA foi definido pelos planos sagital, coronal e axial. O sistema de grade de Bernard e Hertel foi utilizado para comparar a posição dos túneis entre os protocolos, utilizando parâmetros para comprimento e altura. Resultados: Houve diferença significativa entre as medidas dos protocolos de renderização de imagem 3D-TC e 3D-TC por transparência para altura (23,8 ± 7,9mm e 33,0 ± 5,0mm, respectivamente; p=0,017), sem diferenças para comprimento (18,6 ± 4,2mm e 18,3 ± 4,5mm, respectivamente; p=0,560). Conclusão: A altura no protocolo de TC por transparência foi diferente e o comprimento foi igual quando comparados com o protocolo 3D-TC por renderização de imagem no método de Bernard e Hertel para mensuração dos túneis. ***Nível de Evidência II, Estudo Laboratorial Descritivo.***

Descritores: *Reconstrução do ligamento cruzado anterior. Imagem tridimensional. Processamento de imagem assistida por computador.*

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INTRODUCTION

Recent research on anterior cruciate ligament (ACL) reconstruction has endorsed restoration of the original anatomy.[1,2] Correct placement of the femoral and tibial tunnels may help restore physiological relationships and ensure near-normal function of the knee joint. Because graft positioning is the most important intraoperative variable for surgical success,[3] accurate analysis of the tunnel position is especially relevant in terms of quality control and improvement in ACL reconstruction.

The quadrant method, originally described by Bernard et al.,[4] is the most commonly used reference for location of the ACL, originally described for the lateral x-ray of the distal femur.[5-7] Gold standard imaging technique for evaluating osseous anatomy of the knee and anatomical femoral tunnel position is the rendering 3D computed tomography (CT) scan.[8-15] However, conventional 3D CT rendering is time consuming and technically demanding. A less demanding open-source 3D CT protocol based on the principles of Bernard and Hertel x-ray method has recently been introduced and suggested for ACL femoral tunnel measurement.[16]

All the authors declare that there is no potential conflict of interest referring to this article.

This study was conducted at the Universidade de São Paulo, Faculdade de Medicina, Departament of Orthopedics and Traumatology, Laboratório de Investigação Médica do Sistema Musculoesquelético, São Paulo, SP, Brazil.
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Therefore, the aim of the present study was to compare the transparent CT image protocol against the conventional 3D CT image rendering protocol. The hypothesis was that these two different protocols would properly evaluate osseous landmarks and femoral tunnel positioning in anatomical ACL reconstruction.

MATERIAL AND METHODS

We evaluated 8 unilateral knee CT scans of cadavers, with the approval of the University of São Paulo Medical School Institutional Review Board (CEP no 436/11). All CT scans were from male subjects with an average age of 63.2 +/- 10.6 years.

All subjects were scanned in supine position from the mid-pelvis to the proximal tibia following the same protocol, using a 64-slice multi-slice spiral CT scanner (LightSpeed Plus, GE Medical Systems, Milwaukee, WI) with 120kV and 80mA settings. The images were acquired along the axial direction with a 1.25 mm slice thickness, in-plane resolution of 0.74 0.74 mm, and matrix size of 512 x 512.

Outside-in anatomic ACL reconstruction technique was used. Tunnels were created by the same senior surgeon in each knee in the center of the original ACL, above the ACL footprint remnants. Tunnels were created but grafts were not positioned, since they were not necessary for the present study.

3D CT image rendering protocol

Bone was rendered from the axial CT slices using Amira software (FEI Visualization Sciences Group, Bordeaux, France),[17,18] processed with Geomagic Studio software (Research Triangle Park, NC) and analyzed with Rhinoceros software (McNeel North America, Seattle, WA). Lateral view was standardized by aligning posterior femoral condyle wall in the sagittal and axial planes and inferior wall in the sagittal and coronal views (in other words, following the protocol by Bird et al.).[9] A coordinate system parallel to this view was created and dislocated to the most superior aspect of the intercondylar notch.[18] (Figure 1A)

Medial femoral condyle using Rhinoceros® tools according to the parallel plane created in the previous step. Central point of the ACL tunnel position was set using the sagittal plane. (Figure 1B)

Transparent 3D CT measurement protocol

Using an open-source software (OsiriX Imaging Software, http://www.osirix-viewer.com), 3D surface models of the femur were reconstructed from CT images (DICOM) using gradient threshold and region growing. Images were acquired including intercondylar notch and lateral condyle in a bone transparent imaging technique similar to radiographies (transparency 3D MPR protocol) available in this software.[16] As mentioned before, posterior femoral condyle walls were aligned in sagittal and axial view and inferior walls in sagittal and coronal views to standardize the lateral view. Central point of the ACL tunnel position was set using sagittal, coronal and axial planes. (Figure 2)

Bernard and Hertel method.

The grid system described by Bernard and Hertel[4] was used to determine the tunnel position. In a lateral view, a line tangent to the roof of the intercondylar notch (Blumensaat's line) was drawn. Two lines were drawn perpendicular to this line, one at the intersection of the tangent line with the shallow border of the lateral femoral condyle and the other with intersection of the tangent line and the deep border of the lateral femoral condyle. Another line parallel to Blumensaat's line and tangent to the inferior border of the condyles was drawn to form the grid. ACL tunnel's central point was measured using height and length parameters. (Figure 3)

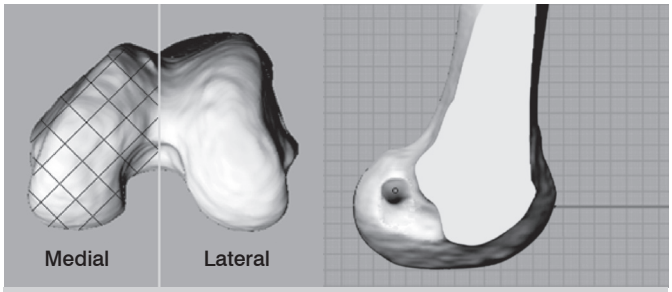

Figure 1. Rendered 3D CT protocol scan using Rhinoceros® software. (A) Axial view, with most superior intercondylar notch plane set. (B) Lateral view after medial condyle was cropped, showing central point of ACL tunnel (green dot) at the medial wall of the lateral condyle.

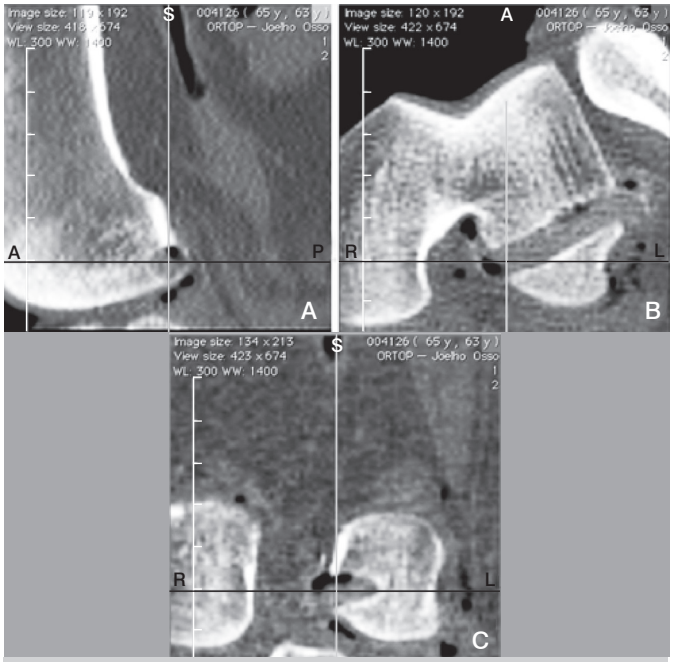

Figure 2. Sagittal (A), coronal (B), and axial (C) views of the central point of the ACL tunnel using OsiriX® Imaging Software.

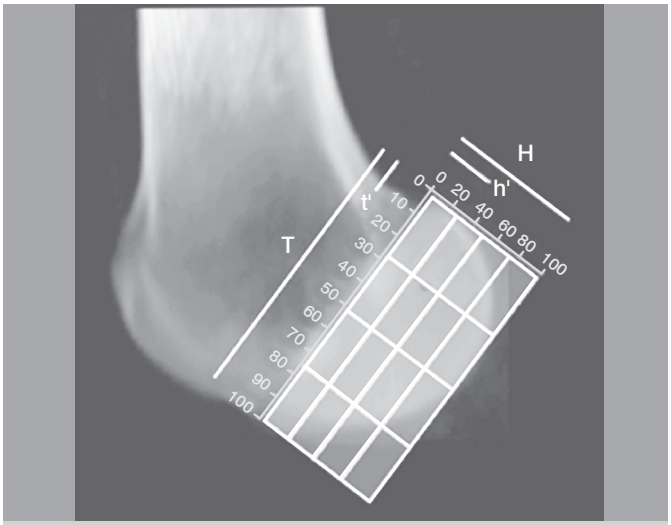

Figure 3. Bernard and Hertel[4] quadrant method in a neutral transparent CT scan of the lateral femoral condyle. T = total condyle length, t' = central ACL percentage of T; H = total height, h' = central ACL percentage of H.

Comparison between both protocols.

The same world coordinate system (WCS) was used for both methods. The central point of the femoral tunnel was projected from one system (OsiriX) to the other (Rhinoceros) onto the lateral condyle. The same lateral view was used again, as described previously.

Distance between the two points was measured utilizing height (H) and length (T) parameters by Bernard and Hertel's method in milimeters +/- standard deviation and absolute distance between tunnels was also measured.

Statistics

We tested data for normality and variance. Because distribution was normal, we performed paired t-tests ($P < 0.05$) using SigmaPlot 12.5 for Windows software. We calculated the sample size and the power of the study starting with the primary outcome.

RESULTS

Both of the compared parameters (length and height) passed the normality test (Shapiro-Wilk); Two-tailed P-value for length was 0.560, and for height was 0.017.

Mean values for lenght (T) measurements using Rhinoceros and OsiriX were 18.6 +/- 4.2 and 18.3 +/- 4.5, respectively ($P = 0.560$). The mean values for height (H) measurements using Rhinoceros and OsiriX were 23.8 +/- 7.9 and 33.0 +/- 5.0, respectively ($P = 0.017$). Figure 4 shows mean localization of ACL tunnel's central point according to both methods (Rhinoceros and OsiriX) and also the distance between the central tunnel position using both methods. Comparison of both methods found a significant difference between groups for height, and no differences for length. (Figure 5)

DISCUSSION

Precise studies of tunnel positions in knees with ACL reconstruction can prevent inaccurate positioning and consequent negative outcomes. Non-anatomical graft placement is one of the most common causes of failure in ACL reconstruction. Marchant et al. found a misplaced femoral or tibial graft tunnel in 107 of 122 (88%) patients with failed ACL reconstructions.[1] The kinematics of the reconstructed knee are altered by the position of the femoral and tibial tunnels. Anatomical ACL reconstruction restores original stability closer to the native ACL and provides better knee kinematics when compared to non-anatomical ACL reconstruction.[19] The clinical relevance of the present study is intimately related to the importance of correct reporting of tunnel positioning to compare post-surgical outcomes in ACL anatomic reconstruction. Van Eck et al.[20] states that outcomes should be reported and compared in a similar and thorough manner for valid interpretation. Post-operative CT investigation of ACL reconstruction has the potential to improve surgical technique and the novel transparent 3D CT imaging protocol can contribute to this outcome.

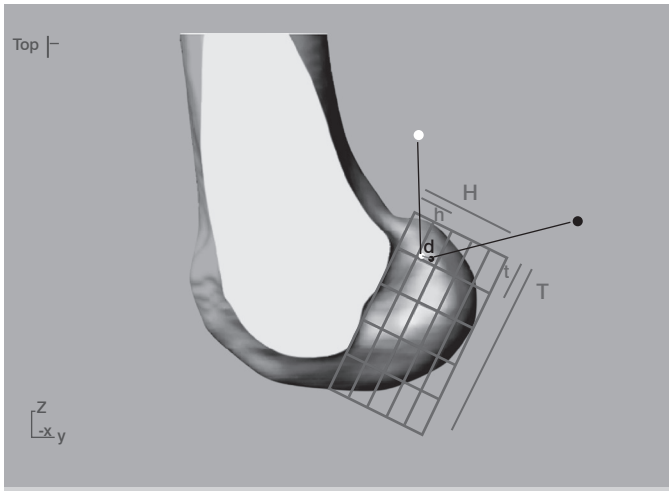

Figure 4. Lateral view of the medial femoral condyle. Red dot indicates mean center of ACL tunnel position using Rhinoceros. Blue dot represents the same position using OsiriX. Note the difference in height (H) between radiological methods. Distance between tunnels (d) = 2.02 mm.

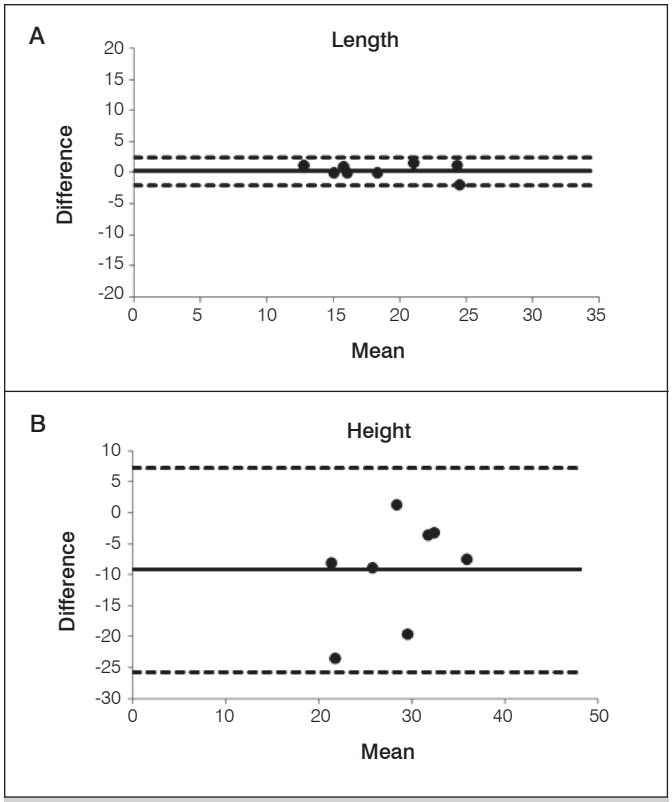

Figure 5. Bland-Altman plots analyzing the agreement of both methods for measuring length (A) and height (B) of femoral ACL tunnels. Y axis shows the difference between the two paired measurements and X axis represents the average of these measures. Solid line represents mean measurement values using both methods and dotted lines represent limits of agreement, from -1.96s to +1.96s. Note high correlation between methods for measuring length, but not for height.

The present study compared two methods for analyzing post-operative femoral tunnel position in ACL reconstruction: the novel transparent 3D CT image protocol and the conventional 3D CT image rendering protocol. This comparison produced similar results for length measurements but different results for height. Consequently, different ACL reconstruction procedures can be compared by properly choosing one of the imaging evaluation methods separately. Surgeons can choose one of the methods to evaluate femoral tunnel positioning in anatomic ACL reconstruction, but they should not compare the methods.

The main advantage of the conventional 3D CT image-rendering protocol is that it is already established and accepted as the preferred method for evaluating femoral ACL tunnel positioning whenever precise measurements are needed.[10] The disadvantage of this method is that it requires specific and consequently more onerous training to correctly assess and interpret data, as well as more expensive software for image processing.

The transparent 3D CT protocol has already been proven to accurately measure the ACL femoral tunnel,[16] and uses an open-source software that requires a lower level of technical skill. However, this tool is chosen less frequently when compared to the conventional 3D CT image-rendering protocol.

Limitations of the present study include assessing only femoral tunnel position but not tibial. Although it is the position of the femoral tunnel that plays a major role in providing graft isometricity, it would be interesting to analyze the tibial tunnel position in future studies; questions related to the measurement of tunnel positions in the coronal and axial planes might also emerge. Measurements were taken only in the lateral view since this is where ACL tunnels are positioned. Furthermore, the tunnel angulation in the coronal and axial planes does not alter knee kinematics to the same degree as variations in the sagittal plane. Finally, height and length parameters were measured but the center angle of the ACL graft was not analyzed. Future studies are proposed to study these parameters, as well as variations with internal and external femoral axis rotation or adduction and abduction of the cropped medial femoral condyle in the rendered CT protocol. These variations should make a difference in measurement outcomes.

CONCLUSION

Height in the transparent 3D CT image protocol was different and length was equal when compared to the 3D CT image-rendering protocol using the Bernard and Hertel method for tunnel measurement.

AUTHORS' CONTRIBUTIONS: Each author made individual and significant contributions to the development of this manuscript. MAB (0000-0003-2181-4698)* was responsible for the conception and design of the project and preparation and drafting of the manuscript. TFL (0000-0002-6665-3608)* was responsible for acquiring and interpreting the data and the statistical analysis. DD (0000-0002-9558-7080)* was responsible for the critical revision of the draft. AP (0000-0002-8449-7493)* was responsible for directing the stages of the project. AJH (0000-0001-8645-3956)* was responsible for final approval. *ORCID (Open Researcher and Contributor ID).

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DOI: http://dx.doi.org/10.1590/1413-785220172501161719

ORIGINAL ARTICLE

MORPHOLOGICAL ANALYSIS OF THE SCAPULA AND ITS IMPLICATIONS IN BRISTOW-LATARJET PROCEDURE

ANÁLISE MORFOLÓGICA DA ESCÁPULA E AS SUAS IMPLICAÇÕES NO PROCEDIMENTO DE BRISTOW-LATARJET

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ABSTRACT

Objective: To assess which of two procedures, Bristow or Latarjet, is anatomically the most appropriate for the general population. Methods: One thousand one hundred and thirty two shoulders were evaluated by an observer who measured the following coracoid process parameters - length, angle and minimum thickness - through Computed Tomography (CT) analysis. Statistical analysis was carried out by ANOVA and Bland-Altman tests. Results: The mean length, angle and minimum thickness of the coracoid were 27.0 ± 3.80 mm; 103.54 ± 14.03°; and 9.16 ± 6.38 mm, respectively. Gender differences were statistically significant. Conclusion: According to this image-based anatomic study, the coracoid process dimensions do not influence the choice between Bristow or Latarjet procedures. ***Level of Evidence III, Therapeutic Studies - Investigating the Results of Treatment.***

Keywords: Shoulder dislocation/etiology. Joint instability. Range of motion, articular. Treatment outcome.

RESUMO

Objetivo: Avaliar qual dos dois procedimentos, Bristow ou Latarjet, é o mais adequado anatomicamente para a população em geral. Métodos: Um mil cento e trinta e dois ombros foram sujeitos à avaliação de vários parâmetros do processo coracóide – comprimento, ângulo e espessura mínima – através da análise de exames de Tomografia Computadorizada (TC). A análise estatística teve por base os testes ANOVA e Bland-Altman. Resultados: As médias obtidas do comprimento, do ângulo e da espessura mínima do processo coracóide foram, respetivamente, 27,00 ± 3,80 mm, 103,54 ± 14,03° e 9,16 ± 6,38 mm. As diferenças obtidas entre gêneros foram estatisticamente significativas. Conclusões: De acordo com o estudo realizado, as dimensões do processo coracóide não constituem um critério para a decisão da opção terapêutica entre os procedimentos em causa, Latarjet e Bristow. ***Nível de Evidência III, Estudos Terapêuticos - Investigação dos Resultados do Tratamento.***

Descritores: *Luxação do ombro/etiologia. Instabilidade articular. Amplitude de movimento articular. Resultado do tratamento.*

Citation: *Silva JDO, Damas CN, Sá MCC, Torres JMCF. Morphological analysis of the scapula and its implications in Bristow-latarjet procedure. Acta Ortop Bras. [online]. 2017;25(1):34-7. Available from URL: http://www.scielo.br/aob.*

INTRODUCTION

The shoulder is the most mobile joint of the human body; as a result of its wide range of movement, the glenohumeral joint is highly susceptible to dislocation. This common injury[1] represents 50% of all joint dislocations.[2] Young men who sustain high-energy injuries to the shoulder are most affected.[3] This condition often occurs in athletes and peaks in the second and sixth decades of life.[4]

Previous studies have shown that coracoid transfer procedures are biomechanically advantageous over other glenoid reconstruction options such as autograft from the iliac crest or the use of allografts because of the additional dynamic stabilizing ''sling'' effect produced by the repositioned conjoint tendon. Consequently, coracoid transfer is considered a good solution for instability-related glenoid defects and even isolated capsulolabral tears.[5]

Two common treatments for anterior dislocations are the Latarjet and Bristow procedures. In the Latarjet procedure the entire coracoid process is transferred so that the inferior surface follows the curved shape of the glenoid and is fixed with two screws, while in the Bristow procedure only the tip of the coracoid process is transferred and is fixed with a single screw to the resected surface in contact with the glenoid.[6-8]

Since both of these techniques consist of coracoid transfer procedures and a significant proportion of patients with this pathology will require surgery,[3] we believe it is important to study the anatomy of the coracoid process to determine which of these two procedures is the most anatomically appropriate for the general population. In this study we measured the length, angle, and minimum thickness of this process.

All the authors declare that there is no potential conflict of interest referring to this article.

Study conducted at Hospital São João Porto, Portugal.
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Article received in 12/12/2015, approved in 08/31/2016.

MATERIALS AND METHODS

Chest CT scans performed at a central hospital for diagnostic purposes during two randomly chosen months (June 9–August 8, 2014) were evaluated by an observer with a master's degree. A total of 566 CT scans were obtained (1132 shoulders). Sixty-six CT scans (11.66%) in which it was not possible to measure the coracoid process were excluded. Exclusion criteria were: repeated subject (N=1, 0.18%), CT scans that did not show the coracoid process (N=54, 9.52%), presence of cartilage growth (N=8; 1.41%), and presence of degenerative changes (N=4; 0.70%). (Table 1) Other exclusion criteria were cases with a history of bone surgery or scapula fracture, but no patients presented these characteristics.
The CT scans were accessed and targeted parameters were measured using a Sectra IDS7 workstation, version 15.1.24.1 @2012 Sectra AB. A total of 500 (88.34%) CT scans in the axial plane were reviewed. In all of these CT scans the coracoid process parameters were measured (length, angle, and minimum thickness). Length was defined as the distance between one point on the apex and another point at the base of the coracoid process. (Figure 1) Four points along the lateral border of the coracoid process demarcated the angle: one at the front end of the medial border, the second and the fourth at the point with the greater curvature, and the third at the base of the coracoid process. (Figure 2) Finally, minimum thickness was defined as the shortest distance between two opposite points on the medial and lateral cortical margins of the coracoid body. (Figure 3) Statistical analysis was performed using Microsoft Excel 2010 and MedCalc 14.12.0 version software. ANOVA was used to analyze the variance between measurements obtained by two researchers working independently. No statistically significant difference was seen between the two researchers, giving power to the method used. Blinded measurements of the two observers and Bland-Altman analysis determined inter-rater reliability. Differences were considered statistically significant at $P<0.05$.
Institutional review board approval was not necessary since we did not intervene in patient care or handle personal data.

Table 1. Exclusion Criteria.

Exclusion Criteria		
Criteria	**Frequency (n)**	**Percent (%)**
Presence of degenerative changes	4	0.70
Presence of growth cartilage	8	1.41
Coracoid process not visible in the CT scans	54	9.52
Repeated subject	1	0.18
Total	66	11.81

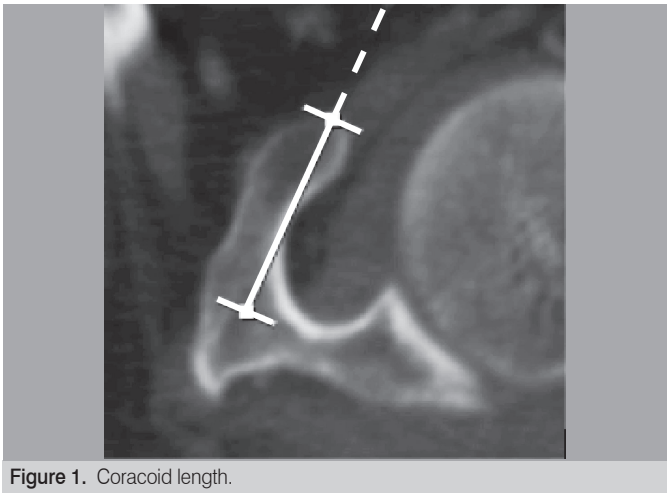

Figure 1. Coracoid length.

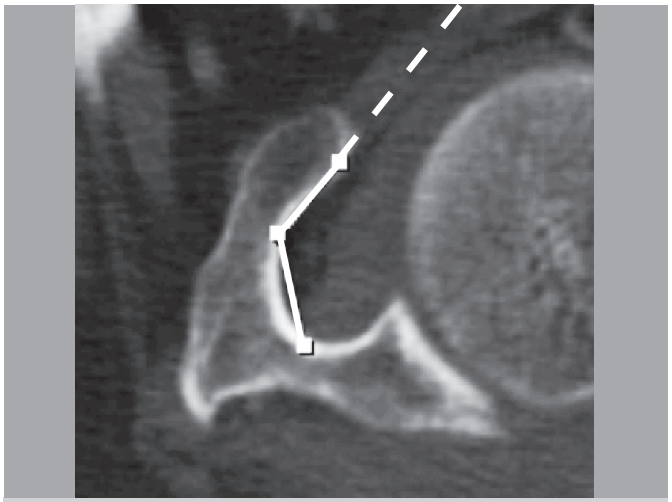

Figure 2. Coracoid angle.

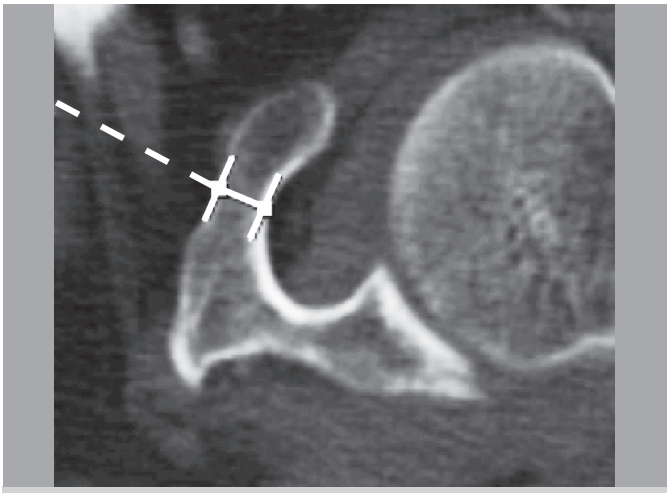

Figure 3. Minimum thickness of the coracoid process.

RESULTS

The CTs from the 500 included subjects (1000 shoulders) comprised 196 (39.20%) female and 304 male (60.80%) subjects with a mean age of 64.15 years (21–95) and 63.64 years (16–93), respectively (IC 95%; P=0.615). (Table 2)
Length: the length was measured in 864 coracoid processes. Mean length was 27.00 ± 3.80 mm, (Table 3) and minimum and maximum values were 17.70 mm and 40.50 mm, respectively. These included 343 female (25.08 ± 2.98 mm) and 521 male (28.25 ± 3.76 mm) subjects (IC 95%; P<0.0001). (Table 4)
Angle: the angle was measured in 917 coracoid processes. The mean angle was 103.54 ± 14.03°, (Table 3) and the minimum and maximum values were 58.1° and 155.30°, respectively. These

Table 2. Included subjects.

Included subjects		
Gender	**Frequency**	**Percent (%)**
Female	196	39.20
Male	304	60.80
Total	500	88.34

Table 3. Data Summary – measurements of the coracoid process.

Parameters	Mean	SD	Minimum	Maximum
Length (mm)	27.00	3.80	17.70	40.05
Angle (º)	103.54	14.03	58.10	155.30
Minimum thickness (mm)	9.16	6.38	5.20	15.80

Table 4. Sex differences.

Sex differences						
Parameters	**Gender**	**Mean**	**SD**	**Minimum**	**Maximum**	**P value**
Length (mm)	Female	25,08	2,98	17,70	35,7	< 0,0001
	Male	28,25	3,76	18,40	40,50	
Angle (º)	Female	101,33	14,26	58,1	143,40	0,0001
	Male	104,96	13,70	62,8	155,30	
Minimum thickness (mm)	Female	8,38	6,53	5,20	15,80	0,003
	Male	9,67	6,24	5,50	14,4	

included 357 female (101.33 ± 14.26º) and 560 male (104.96 ± 13.70º) subjects (IC 95%; P=0.0001). (Table 4)

Minimum thickness: minimum thickness was measured in 916 coracoid processes; the mean minimum thickness was 9.16 ± 6.38 mm, (Table 3) and the minimum and maximum values were 5.20 mm and 15.80 mm, respectively. The subjects were 362 females (8.38 ± 6.53 mm) and 554 males (9.67 ± 6.24 mm) (IC 95%; P=0.003). (Table 4)

Gender differences were statistically significant; as expected, scans of the female subjects exhibited lower mean lengths and minimum thickness. (Table 4)

DISCUSSION

Since the dimensions of the shoulder blades vary according to different populations, one limitation of this study is that the sample population may not be representative of the global population. Additionally, since the CT scans were not performed to evaluate the shoulder blade, not all scans allowed us to properly evaluate the coracoid.

Other studies have quantified the size of the coracoid process; none were carried out expressly for this purpose, however, and do not contain as many cases as we evaluated in this study.

In previous studies, the results for the length of the coracoid process varied significantly according to the type of assessment: namely, measurements taken from cadavers varied more than measurements from studies involving x-rays, which presented values closer to those obtained in this study.[5,9,10] The minimum thickness of the coracoid process did not vary as much and were similar to our findings.[5,9,10] No comparable studies measured the angle of the coracoid process using the definition applied in this study.

The most commonly used screws in the Latarjet or Bristow procedures are 35-mm 4.5-mm partially threaded malleolar screws.[11] Considering these screw dimensions and the mean, maximum, and minimum values for length and minimum thickness found in this study, we can conclude that the coracoid process demonstrated thickness sufficient to support 1 screw and length sufficient to support 2 screws. Characterization of the angle of the coracoid process is important, since it permits a three-dimensional concept during the surgery; consequently, it appears that the Latarjet or Bristow procedures can be formed interchangeably based on these parameters.

A low rate of recurrence using different variations of the Latarjet or Bristow procedures was reported in several studies[12-17] which also demonstrated favorable long-term results.[7,10,12] Coracoid transfer procedures are especially indicated in recurrent anterior dislocations associated with hyperlaxity or glenoid bone loss. In situations featuring voluntary anterior instability or anterior instability without a Bankart lesion these procedures are not recommended. Two common complications of these procedures are non-union of the coracoid process (more common in the Bristow procedure due to the instability resulting from single screw fixation and less bone contact between surfaces) and intra-articular positioning of the graft (more common in the Latarjet procedure due to the larger size of the graft).[18]

Considering that this study revealed that the dimensions of the coracoid process are not relevant criteria for selecting the best surgical option, it seems important to study the glenoid anatomy before choosing a procedure; anterior shoulder instability is frequently associated with glenoid bone loss, which varies greatly in both extent and significance.[11,19-21]

CONCLUSION

This image-based anatomic study shows that the dimensions of the coracoid process do not determine whether the Latarjet or Bristow procedures are better choices for surgical treatment. The glenoid anatomy is an important target for further study.

AUTHORS' CONTRIBUTIONS: Each author made significant and individual contributions to the development of this manuscript. JMCFT (0000-0001-9927-1158)* and JDOS (0000-0001-8591-2807)* were the main contributors in drafting this article. CND (0000-0001-8640-0280)* and JDOS collected the clinical data. MCCS (0000-0003-4084-2037)* evaluated the data for statistical analysis. JMCFT and JDOS conducted the bibliographic research, revised the manuscript, and contributed to the intellectual concept of the study. *ORCID (Open Researcher and Contributor ID).

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ORIGINAL ARTICLE

ALLOGENEIC PLATELET-RICH PLASMA FOR ROTATOR CUFF REPAIR

PLASMA RICO EM PLAQUETAS ALOGÊNICO PARA REPARO DO MANGUITO ROTADOR

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ABSTRACT

Objective: To investigate the safety and efficacy of allogeneic platelet-rich plasma (PRP) in rotator cuff repair. Methods: Seventeen patients with a full-thickness rotator cuff tear were included. Ten patients underwent arthroscopic rotator cuff repair with allogeneic, and seven patients with autologous PRP. Three PRP gels in a volume 3 ml each were applied between the torn end and the greater tuberosity. Clinical outcomes were assessed preoperatively and at a minimum of 2 years after surgery. Structural outcomes were evaluated with the presence of retear and the change of the cross-sectional area (ACT) of the supraspinatus. Results: Allogeneic PRP did not cause any adverse events during the follow-up period. There was no significant difference in the clinical outcome measures between the two groups (all $p > 0.05$). The retear rate was 33.3% and 25.0% in the allogeneic group and autologous group, respectively ($p = 0.764$). The change between the one-year postoperative and immediately postoperative ACT was not also significantly different between the two groups ($p = 0.373$). Conclusion: Allogeneic PRP in arthroscopic rotator cuff did not cause any local or general complications and that has the efficacy comparable to autologous PRP with respect to the clinical and structural outcomes. ***Level of Evidence III, Retrospective Comparative Study.***

Keywords: Platelet-rich plasma. Rotator cuff. Growth factors. Tendon injuries.

RESUMO

Objetivo: Investigar a segurança e eficácia do plasma rico em plaquetas alogênico (PRP) no reparo do manguito rotador. Métodos: Foram incluídos dezessete pacientes com ruptura da espessura total do manguito rotador. Dez pacientes foram submetidos a reparo artroscópico do manguito rotador com PRP alogênico e sete pacientes com PRP autólogo. Três géis de PRP de 3ml cada foram aplicados entre a extremidade lesionada e a tuberosidade maior. Os resultados clínicos foram avaliados no pré-operatório e no mínimo 2 anos após a cirurgia. Os resultados estruturais foram avaliados com a presença de nova ruptura e a alteração da área em corte transversal (ACT) do supra-espinhal. Resultados: O PRP alogênico não causou quaisquer eventos adversos durante o período de acompanhamento. Não houve diferença significativa nas medidas de resultados clínicos entre os dois grupos (todos os valores p> 0,05). A taxa de nova ruptura foi de 33,3% e 25,0% no grupo alogênico e grupo autólogo, respectivamente (p = 0,764). A alteração da ACT entre o pós-operatório de um ano e imediatamente no pós-operatório também não foi significativamente diferente entre os dois grupos (p = 0,373). Conclusão: O PRP alogênico administrado por via artroscópica no manguito rotador não causou quaisquer complicações locais ou gerais e sua eficácia é comparável ao PRP autólogo no que diz respeito aos resultados clínicos e estruturais. ***Nível de Evidência III, Estudo Retrospectivo Comparativo.***

Descritores: *Plasma rico em plaquetas. Bainha rotadora. Fatores de crescimento. Traumatismos dos tendões.*

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INTRODUCTION

Platelet-rich plasma (PRP) has recently been actively investigated in various injuries and diseases.[1] While the effects of PRP in arthroscopic rotator cuff repair have also been reported by several authors,[2-4] the results are still not conclusive. Most of the previous studies used autologous PRP,[1,5,6] but this plasma may not be available in certain patients such as patients with hematological diseases or who use anti-platelet medication, elderly patients with multiple comorbidities, patients who do not want to draw blood for any reason, and so on.[7,8] Even though percutaneous local delivery of PRP improved fracture healing in diabetic rats,[9] autologous PRP might not be an optimal solution since it has been reported that expression of platelet-derived growth factor decreased in diabetic animals.[10] Therefore, an alternative to

All the authors declare that there is no potential conflict of interest referring to this article.

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autologous PRP in these circumstances may be necessary, and allogeneic PRP is an option. Allogeneic platelets in the form of platelet concentrates have long been given safely in the treatment of thrombocytopenia or platelet dysfunction, or to patients with active platelet-related bleeding, or as prophylaxis in patients without cross-matching who are at serious risk of bleeding. Besides transfusion medicine, use of allogeneic PRP has only been described in a few case reports of oral and maxillofacial surgery.[8,11,12] No study was found in the field of orthopedics except for one case report on the treatment of pseudoarthrosis of the distal tibia in a diabetic patient.[8]

The goal of this retrospective cohort study was to investigate the safety and efficacy of allogeneic PRP application in arthroscopic rotator cuff repair with regards to the clinical and structural outcomes. Our hypothesis was that allogeneic PRP was as safe and effective as autologous PRP.

PATIENTS AND METHODS

Study design and patients

This retrospective cohort study was approved by the hospital's institutional review board (IRB of Seoul National University Boramae Medical Center, No. 262015112). We investigated clinical and structural outcomes in patients who underwent arthroscopic rotator cuff repair with allogeneic PRP in comparison with patients who received autologous PRP. All allogeneic PRP was obtained from patients who underwent arthroscopic rotator cuff repair with autologous PRP on the same day. The inclusion criteria were full-thickness rotator cuff tear treated by arthroscopic rotator cuff repair with allogeneic PRP and minimum follow-up of 24 months.

From March 2009 to March 2011, 10 patients underwent arthroscopic rotator cuff repair with allogeneic PRP that was drawn and prepared from 8 patients who also underwent surgeries with autologous PRP on the same day; 4 with full-thickness rotator cuff tears and 3 with partial-thickness tears underwent rotator cuff repair, and 1 with a refracture of the clavicle and a metal failure received open reduction revision and internal plate fixation. Among the 10 patients who received allogeneic PRP, 6 received plasma from 6 different patients (5 with rotator cuff tears and 1 with a refracture), and the other 4 received plasma from 2 patients (2 from each one patient with a partial-thickness rotator cuff tear). Therefore, a total of 17 patients were included in the study: 10 in the allogeneic group, and 7 in the autologous group.

Preparation of PRP

PRP was obtained one day before surgery using a plateletpheresis system with a leukoreduction set (COBE Spectra LRS Turbo, Caridian BCT, Lakewood, Colorado) as previously described.[2] An aliquot was used to determine complete blood counts using a fully automated analyzer (XE- 2100, Sysmex Corporation, Kobe, Japan), and concentration of fibrinogen was assessed using an automated coagulation analyzer (CA-7000, Sysmex Corporation). For use in the rotator cuff repair, the platelet counts in the PRP were adjusted with saline to 1000 x 10^3 platelets per microliter. To produce a gel from the prepared PRP, 0.3 ml of 10% calcium gluconate was added to 3 ml of PRP. The dilution and gelling procedure was performed within one hour of surgical application.[2]

To assess the safety of the allogeneic PRP, tests for hepatitis B (HBV), hepatitis C (HCV), human immunodeficiency virus (HIV), and syphilis (VDRL) were performed and confirmed before application.[12]

Surgical procedures and application of PRP

Arthroscopic surgery and application of PRP were performed with patients in the lateral decubitus position under general anesthesia, as described previously.[13,14] Three PRP gels per patient were threaded to the suture and introduced into the 5.5 mm cannula after medial row sutures were placed. With the PRP gels in place, medial row sutures were tied using a SP knot if necessary.[15] The lateral row was then secured using suture anchors, and the PRP gels were interposed at the tendon-bone interface. The patient's shoulders were immobilized for four to six weeks using an abduction brace and then passive range of motion (ROM) and active assisted ROM exercises were gradually permitted. Patients began strengthening exercises after three months.

Outcome assessments

For the safety evaluation, general symptoms or signs related to immune responses such as fever, chills, pruritis, dyspnea, urticaria, or rash were observed. The wound site was also evaluated daily to determine the presence of zones of erythema, swelling, or abnormal discharge until patients were discharged from the hospital.

Clinical outcomes were assessed according to: 1) pain, 2) ROM, 3) muscle strength, 4) overall satisfaction, and 5) functional scores. To evaluate structural integrity, magnetic resonance imaging (Achieva 3.0-T, Philips Medical System, Eindhoven, The Netherlands) with a dedicated shoulder coil was performed at least 9 months after surgery. Structural integrity was evaluated using Sugaya's MRI classification for patients.[16] All images were reviewed by a fellowship-trained musculoskeletal radiologist and an orthopedic surgeon. The change in the cross-sectional area (CSA) of the supraspinatus was calculated by subtracting measures of the two different time points.[17-19] The statistical analysis was performed using SPSS version 13.0 (SPSS Inc., Chicago, IL), and the significance level was set at $p=0.05$ throughout.

RESULTS

Baseline demographics & adverse events

All 17 patients were followed clinically for a minimum of 24 months. The average age was significantly higher in the allogeneic group (63.57 ± 9.61) than in the autologous group (56.33 ± 7.45), and there were more women in the allogeneic group (80.0%) than in the autologous group (28.6%). All patients in the allogeneic group had a full-thickness rotator cuff tear, while 3 of 7 (42.9%) in the autologous group had a partial-thickness rotator cuff tear ($p = 0.023$). The other characteristics did not differ significantly, as summarized in Table 1.[20] No general or local adverse events with regard to allogeneic or autologous PRP usage were observed during the immediate postoperative or follow-up periods.

Characteristics of PRP with respect to concentration, activation, and method of application

The characteristics of the PRP used in this study are described using the CAM classification.[21] (Table 2) The average platelet count increased from 256.71 ± 72.04 (x 10^3 platelets per microliter) in whole blood to 918.14 ± 149.61 in PRP, a 3.6-fold increase from the baseline ($p < 0.001$). The average red and white blood cell counts fell from 4.44 ± 0.48 to 0.15 ± 0.07 (x 10^3 cells per microliter), and from 5.59 ± 0.68 in whole blood to 0.02 ± 0.01, respectively, representing a 0.03- and 0.004-fold decrease from the baseline, respectively (all $p < 0.001$).

Table 1. Baseline demographics.

	Allogeneic (n=10)	Autologous (n=7)	p-value
Mean age, y	63.57 9.61	56.33 7.45	0.029
Sex (male:female), n	2:8	5:2	0.034
Side (right:left), n	8:2	5:2	0.682
Dominance (yes:no), n	7:3	5:2	0.949
Duration, mo	14.40 13.02	21.71 19.46	0.366
Aggravation, mo	2.71 1.38	3.42 3.17	0.604
fRCT : pRCT, n	10:0	4:3	0.023
None: SLAP I : SLAP II+, n	7:2:1	6:0:1	0.450
SB tear grade (0:1:2:3)*, n	2:6:1:1	2:3:1:1	0.922
Biceps tear (none: partial : complete), n	6:3:1	3:3:1	0.784
Cofield type (P:S:M:L:MSV), n	0:1:5:3:1	3:0:1:1:2	0.103
Boileau stage (I:II:III:IV), n	4:1:4:1	3:1:1:2	0.614
Tendon grade (A:B:C)†, n	1:6:3	3:3:1	0.279
Treatment (StoS: 1 row : 2 row), n	1:1:8	2:1:4	0.556
Labrum (none : debride : repair), n	7:3:0	6:0:1	0.160
SB (none: debride : repair), n	3:5:2	2:2:3	0.551
Biceps (none: tenodesis : debride : tenotomy), n	7:0:3	4:1:2	0.464
Acromioplasty (yes:no), n	1:9	0:7	0.388
GT medialization (yes:no), n	1:9	2:5	0.323
GT coverage (A:B:C:D)‡, n	4:5:0:1	3:3:1:0	0.536
Fatty infiltration (0:1:2:3:4), n			
Supraspinatus	0:5:1:2:2	3:1:1:1:1	0.200
Infraspinatus	1:5:2:1:1	3:2:2:0:0	0.423
Subscapularis	4:6:0:0:0	3:3:0:1:0	0.435
GFID	1.43 0.88	1.05 0.80	0.370
Muscle atrophy			
Tangent (1:2:3)§, n	6:3:1	4:3:0	0.638
Occupation ratio (1:2:3)‖, n	4:4:2	4:1:2	0.519
Clinical follow-up, mo	29.57 5.97	28.29 5.59	0.946
MRI follow-up, mo	15.00 3.94	10.50 1.91	0.053

*Subscapularis tear was graded according to the Nove-Josserand et al.[20] Grade 0, normal tendon; grade 1, tear less than one-quarter; grade 2, tear more than one-quarter but not complete; and grade 3, complete tear †Tendon grade assesses rotator cuff quality using three gross tendon criteria;[14] (1) fraying over half of the tendon thickness; (2) delamination of the supraspinatus tendon, and (3) thinning of less than half of the normal thickness. A, none of these criteria were met; B, fraying or delamination was identified; and C, both fraying and delamination or thinning regardless of the other criteria ‡GT coverage evaluates the repair quality. A, complete coverage of the original footprint; B, incomplete coverage more than half of the footprint; C, incomplete coverage less than half of the footprint; and D, the presence of defect into the glenohumeral joint §Tangent sign assesses muscle atrophy of the supraspinatus. Grade 1, negative, which means that the superior border of the supraspinatus was superior to the line tangential to the coracoid and scapular spine; grade 2, borderline, which means that the superior border was located about the tangential line; grade 3, positive, which means that the superior border was inferior to the tangential line. ‖Occupation ratio means the ratio of the CSA of the supraspinatus to the fossa. Grade 1, 0.6 to 1; grade 2, 0.4 to 0.6; grade 3, < 0.4. fRCT a full-thickness rotator cuff tear, pRCT a partial-thickness rotator cuff tear, SLAP II+ superior labral anterior and posterior lesion 2 and above, SB subscapularis, P:S:M:L:MSV small:medium:large:massive, StoS side-to-side repair, GT greater tuberosity, GFDI global fatty degeneration index

Table 2. Characteristics of the Platelet-Rich Plasma used in the study with respect to concentration, activation, and method of application

Concentration	**Platelets, 10^3/L**	**WBC, 10^3/L**	**RBC, 10^3/L**	**Fibrinogen, mg/dL**
	918.14 ± 149.61	0.02 ± 0.01	0.15 ± 0.07	NA
Activation	**Activation status (%)***		**Activation method**	
	NA		calcium alone	
Method	**State**	**Volume (ml)**	**Number**	**Interval (day)**
	gel	3x3	1	0

Data are expressed as average ± standard deviation in concentration properties. *Activation status was measured using flow cytometry with CD 61 and CD 62P in five patients. Results were expressed by the percentage of CD 62P-positive counts over CD 61-positive counts. WBC White blood cells, RBC Red blood cells, NA Not available

After surgery, all VAS pain measurements decreased significantly in both groups, and there were no significant differences between the two groups preoperatively or postoperatively. (Table 3) Representatively, average VAS pain measurements decreased from 5.41 ± 2.19 to 0.49 ± 0.69 in the allogeneic group ($p < 0.001$), and from 3.50 ± 1.97 to 0.08 ± 0.17 in the autologous group ($p = 0.010$). Forward flexion, abduction, and internal rotation significantly increased while external rotation of the arm at the side did not increase in the allogeneic group. (Table 3) In the autologous group, external arm rotation at the side significantly increased, while forward flexion, abduction, and internal rotation did not. No significant differences were found between the two groups for active forward flexion, abduction, external arm rotation at the side, and internal rotation before and after surgery.

Supraspinatus strength improved significantly in the allogenic group, from 4.12 ± 3.03 lb to 8.06 ± 2.60 lb ($p = 0.016$), but this was not the case for the autologous group, which showed a less notable improvement from 6.46 ± 3.34 lb to 9.31 ± 4.55 lb ($p = 0.128$). (Table 3) Infraspinatus strength did not significantly improve in either groups, increasing only slightly from 6.80 ± 3.02 lb to 7.93 ± 2.05 lb in the allogeneic group ($p = 0.318$) and from 6.41 ± 2.96 lb to 9.37 ± 4.55 lb in the autologous group ($p = 0.088$). Subscapularis strength improved significantly from 6.10 ± 2.37 lb to 11.29 ± 3.77 lb in the allogeneic group ($p = 0.001$), but not in the autologous group, which increased from 8.77 ± 5.11 lb to 13.90 ± 5.84 lb ($p = 0.138$). The strength of the supraspinatus, infraspinatus, and subscapularis did not differ significantly in the two groups preoperatively or postoperatively.

Eight out of 10 patients (80.0%) in the allogeneic group expressed willingness to undergo surgery again and wouldrecommend the surgery to other patients; in the autologous group this number was 6 (85.7%) and 7 (100.0%) out of 7 patients, respectively, showing no difference between the two groups. (Table 3) Overall function improved from 4.30 ± 2.36 to 8.57 ± 1.51 in the allogeneic group ($p < 0.001$), and from 5.67 ± 1.21 to 9.10 ± 1.18 in the allogeneic group ($p = 0.001$). Overall satisfaction was 88.57 ± 13.45 in the allogeneic group, and 92.14 ± 9.06 in the autologous group.

ASES, Constant, DASH, SST, and SPADI scores significantly improved after surgery, while the UCLA score did not improve in either group. (Table 4) No significant differences were found in all the scores between the two groups both preoperatively and postoperatively.

Table 3. Pain, ROM, Strength and Overall Satisfaction

Variable	Allogeneic (n=10)	Autologous (n=7)	p-value
Pain at rest			
Preop	4.10 ± 1.66	3.33 ± 2.34	0.455
Final	0.29 ± 0.76	0.00 ± 0.00	0.219
p-value	<0.001	0.017	
Pain in motion			
Preop	6.33 ± 3.09	4.00 ± 2.37	0.136
Final	0.62 ± 0.73	0.10 ± 0.16	0.387
p-value	0.001	0.011	
Pain at night			
Preop	5.80 ± 2.78	3.17 ± 2.71	0.086
Final	0.57 ± 0.79	0.14 ± 0.38	0.331
p-value	0.001	0.048	
Pain average			
Preop	5.41 ± 2.19	3.50 ± 1.97	0.102
Final	0.49 ± 0.69	0.08 ± 0.17	0.317
p-value	<0.001	0.010	
Forward flexion, deg			
Preop	131.00 ± 36.73	165.71 ± 29.36	0.056
Final	175.00 ± 7.64	174.29 ± 7.87	0.960
p-value	0.005	0.448	
Abduction, deg			
Preop	122.00 ± 45.59	160.00 ± 44.35	0.108
Final	174.29 ± 15.12	177.14 ± 7.56	0.658
p-value	0.005	0.360	
External rotation arm at side, deg			
Preop	41.00 ± 15.06	45.71 ± 14.56	0.529
Final	46.43 ± 17.01	58.57 ± 16.26	0.102
p-value	0.635	0.022	
Internal rotation, vertebral level			
Preop	7.70 ± 3.86	9.14 ± 3.53	0.445
Final	11.57 ± 1.40	10.86 ± 1.57	0.628
p-value	0.020	0.127	
Supraspinatus, lb			
Preop	4.12 ± 3.03	6.46 ± 3.34	0.154
Final	8.06 ± 2.60	9.31 ± 4.47	0.679
p-value	0.016	0.128	
Infraspinatus, lb			
Preop	6.80 ± 3.02	6.41 ± 2.96	0.797
Final	7.93 ± 2.05	9.37 ± 4.55	0.421
p-value	0.318	0.088	
Subscapularis, lb			
Preop	6.10 ± 2.37	8.77 ± 5.11	0.165
Final	11.29 ± 3.77	13.90 ± 5.84	0.200
p-value	0.001	0.138	
Surgery again, n (%)			
Final	8 (80.0)	6 (85.7)	0.761
Recommend surgery, n (%)			
Final	8 (80.0)	7 (100.0)	0.208
Overall function			
Preop	4.30 ± 2.36	5.67 ± 1.21	0.212
Final	8.57 ± 1.51	9.10 ± 1.18	0.199
p-value	<0.001	0.001	
Overall satisfaction			
Final	**88.57 ± 13.45**	**92.14 ± 9.06**	**0.353**

Postoperative MRI or CTA was performed in 14 of 17 patients in the study (82.4%): 10 patients (100.0%) in the allogeneic group, and 4 patients (57.1%) in the autologous group. (Table 5) The mean MRI follow-up was 15.00 ± 3.94 months (range 9–20) in the allogeneic group and 10.50 ± 1.91 months in the autologous group. One patient in the allogeneic group was excluded from analysis of structural integrity because rotator cuff repair was done only partially because of limited excursion. Therefore, 9 patients in the allogeneic group and 4 patients in the autologous group were included in the analysis. The retear rate did not differ significantly between the two groups: 33.3% (3 of 9) in the allogeneic group, and 25.0% (1 of 4) in the autologous group (p = 0.764).

Table 4. ASES, Constant, UCLA, DASH, SST, and SPADI Scores.

Variable	Allogeneic (n=10)	Autologous (n=7)	p-value
ASES			
Preop	42.28 ± 23.22	63.06 ± 17.49	0.080
Final	92.77 ± 6.86	98.65 ± 2.00	0.228
p-value	<0.001	0.005	
Constant			
Preop	43.32 ± 19.21	56.70 ± 12.35	0.152
Final	76.35 ± 7.52	82.03 ± 4.96	0.162
p-value	0.001	0.001	
UCLA			
Preop	26.43 ± 18.27	19.97 ± 6.15	0.421
Final	32.29 ± 3.50	28.57 ± 12.93	0.808
p-value	0.868	0.256	
DASH			
Preop	49.75 ± 27.16	31.19 ± 23.97	0.167
Final	6.19 ± 6.65	1.67 ± 2.31	0.190
p-value	0.002	0.017	
SST			
Preop	5.10 ± 3.38	7.33 ± 3.44	0.225
Final	11.29 ± 1.25	11.86 ± 0.38	0.263
p-value	0.001	0.017	
SPADI			
Preop	54.91 ± 28.62	37.10 ± 23.13	0.219
Final	6.14 ± 5.65	0.99 ± 1.81	0.308
p-value	0.001	0.015	

Data are expressed as mean ± standard deviation.

Table 5. Retear Rates.

	Allogeneic (n=9)	Autologous (n=4)	p-value
Retear	3 (33.3%)	1 (25.0%)	0.764

Data are expressed as n (%). PRP, Platelet-Rich Plasma

Supraspinatus CSA taken immediately after surgery and one-year postoperative differed between the two groups; (Table 6) The CSA in the autologous group were greater than those in the allogeneic group at each time point. However, the change between the one-year postoperative and immediate postoperative CSA was not significantly different between the two groups: -67.42 ± 58.75 mm^2 in the allogeneic group, and -49.05 ± 58.57 mm^2 in the conventional group (p = 0.373).

Table 6. Change in the Cross-Sectional Area (CSA) of the Supraspinatus 1 Year after Rotator Cuff Repair.

Cross-sectional area, mm	Allogeneic (n=9)	Autologous (n=4)	p-value
Immediately postoperative	376.77 ± 63.53	478.66 ± 99.63	0.045
One-year postoperative	309.35 ± 69.04	429.61 ± 108.45	0.032
Δ(PO1yr-ImPO)*	-67.42 ± 58.75	-49.05 ± 58.57	0.373

Data are expressed as mean ± standard deviation. *Δ(PO1yr-ImPO), a change of the cross-sectional area of the supraspinatus between the 1-year postoperative measure and immediate postoperative measures.

DISCUSSION

This study showed that allogeneic PRP application in arthroscopic rotator cuff repair did not cause any adverse events, but demonstrated efficacy in clinical and structural outcomes comparable with autologous PRP for the first time, to our knowledge. While many studies have been performed to determine the effect of PRP in various injuries and diseases,[1,2,22] most used autologous plasma, except for a few case reports.[7,8,11,23] Except for one *in vitro* study which investigated the effect of allogeneic PRP compared to autologous PRP,[24] no clinical studies have compared the safety and efficacy of allogeneic PRP over autologous PRP. Therefore, based on findings of this study, we suggest that allogeneic PRP may be a viable alternative when autologous PRP is not available or is less appropriate. However, before allogeneic PRP is used widely in the field of regeneration medicine, we also suggest that safety issues including bacterial or viral disease transmission and immune reaction be further clarified to guarantee patient safety, even though platelet transfusion via platelet pheresis is a safe and standard method undertaken within a highly-developed regulatory environment in blood donation services. For example, the use of a leukoreduction set may be an option, as in the current study,[8] and some kinds of pathogen reduction technologies may merit consideration.[25]

An important cause of controversial results of PRP in rotator cuff repair derives from the wide variability of PRP used in these studies,[26] resulting from different concentrations of cells, activation status, and application method through different preparation systems. Therefore, if these differences could be removed or avoided the real effects of PRP in rotator cuff repair could be more clearly elucidated. In this sense, allogeneic PRP may have several advantages over autologous PRP. First, as a standard blood bank product, a single-donor PRP is very easy to obtain, safe, and would be available in large quantities and incur less cost.[8,11,27] Second, the collection process for this product is well-established and highly standardized with regard to the use of anticoagulant, separation and processing techniques, centrifugal force, and temperature and time, resulting in highly predictable amount of platelets, white blood cells, red blood cells, and fibrinogen. Third, standardized preparation process and products may allow researchers to investigate the effects of PRP more clearly, and the results from various studies could be compared more easily. Additionally, a more standardized method of obtaining allogeneic PRP, such as the platelet pheresis used in this study, would cause less activation of platelets during preparation than manual separation methods.[27,28] Finally, the PRP could be prepared from younger patients in better health. Taken together, allogeneic PRP may have a great potential as a useful tool for biologic treatment strategies and could prove valuable clues to understand the mechanism of PRP, which has not yet occurred with autologous plasma.

One of the strengths of this study was that the patients in the comparison group were the corresponding donors of allogeneic PRP who also underwent the same surgery on the same day. This setting of the study eliminates some concerns about the potential variability of allogeneic PRP, surgical techniques, etc., thus making the results of the study more valuable. Another strength was that the allogeneic PRP was not manufactured and stored for a certain time, but freshly manufactured one day prior to surgery and was used the next day during the procedure, just like autologous PRP. This might be also helpful for removing any possible effects of storing PRP.

Limitations of the present study include; 1) small number of relatively heterogenic participants with regard to age, sex, and patients with partial-thickness rotator cuff tear in the control group, which may increase the risk of a type II error, 2) a lack of randomization, 3) incomplete characterization of PRP, such as absence of activation level or concentration of important growth factors, 4) low MRI follow-up rate to assess retearing, and 5) potential risk of adverse events related to transmission of viral and non-viral immunological infections despite HBV, HCV, HIV, and VDRL screening and use of a leukoreduction set.

CONCLUSION

Allogeneic PRP in arthroscopic rotator cuff repair did not cause any local or general complications and has an efficacy comparable to autologous PRP with respect to clinical and structural outcomes. This study provides the first evidence of the safety and efficacy of allogeneic PRP in arthroscopic rotator cuff repair. Further randomized clinical trials should be performed to support this preliminary study of allogeneic PRP for rotator cuff repair.

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ORIGINAL ARTICLE

EPIDEMIOLOGICAL STUDY ON LISFRANC INJURIES

ESTUDO EPIDEMIOLÓGICO DAS LESÕES DE LISFRANC

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ABSTRACT

Objective: To analyze the characteristics of patients with Lisfranc injuries and their associated fractures. Methods: This is a retrospective analysis on 42 patients with Lisfranc injuries hospitalized at Instituto de Ortopedia e Traumatologia do Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo, between 2006 and 2010. Parameters on patient profile, risk factors, fracture characteristics, data on treatment and acute complications were analyzed. Results: Analysis of 42 cases showed that in our sample, men were more affected than women, with a ratio of 4.25:1. The most frequent trauma mechanism was car accident, followed by motorcycle accident. The most frequent type of injury was isolated lesion type B of Quenu and Kuss classification, representing 50% of cases. The most common fracture on the sample was the second metatarsal bone, with 16 cases, followed by cuboid bone fracture. Among the 42 cases, 17% had exposed fractures and 33 patients presented other associated fractures. The mean time elapsed between the trauma and definitive treatment was 6.7 days, while the mean length of hospital stay was 13.8 days. Six patients presented acute postoperative complications. Conclusion: Lisfranc injuries are more common in men undergoing automobile trauma. The prevalence of associated fractures is a frequent finding and the hospital stay may be longstanding. ***Level of Evidence IV, Case Series.***

Keywords: Tarsal joints/injury. Metatarsal bones/injuries. Foot injuries/surgery. Dislocations/surgery.

RESUMO

Objetivo: Analisar o perfil de pacientes com lesões de Lisfranc, as características das lesões e fraturas associadas. Métodos: Trata-se de uma análise retrospectiva com 42 pacientes com lesões de Lisfranc internados no Instituto de Ortopedia e Traumatologia do Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo entre 2006 e 2010. O perfil dos pacientes, características das lesões, fraturas associadas, dados sobre o tratamento e complicações agudas foram analisados. Resultados: Nesta amostra, os homens foram mais afetados do que as mulheres, com uma proporção de 4,25:1. O mecanismo de trauma mais frequente foi acidente de carro, seguido por acidente com moto. O tipo de lesão mais frequente foi a lesão isolada tipo B de Quenu e Kuss, representando 50% dos casos. A fratura mais comumente encontrada foi a do segundo metatarso, com 16 casos, seguido pela fratura do osso cubóide. Entre os 42 casos estudados, sete foram fraturas expostas e 33 pacientes apresentaram fraturas associadas. O tempo médio entre o trauma e o tratamento definitivo foi de 6,7 dias. O tempo médio de permanência hospitalar foi de 13,8. Seis pacientes apresentaram complicações pós-operatórias agudas. Conclusão: As lesões de Lisfranc são mais comuns em homens submetidos a trauma automobilístico. A prevalência de fraturas associadas é um achado frequente e o tempo de permanência hospitalar pode ser prolongado. ***Nível de Evidência IV, Série de Casos.***

Descritores: *Articulações tarsianas/lesões. Ossos do metatarso/lesões. Traumatismos do pé/cirurgia. Luxações/cirurgia.*

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INTRODUCTION

The term Lisfranc injury is used to refer to injuries involving damage to the tarsometatarsal joint. The term covers a broad spectrum of injuries ranging from damage to the ligaments alone to fractures and fracture-dislocations. Retrospective studies have shown that up to one-third of these injuries go unnoticed during initial assessment.[1-5] According to the literature, Lisfranc injuries are more common around the third decade of life, and are 2-4 times more common in men. Nevertheless, Lisfranc injuries are relatively uncommon, representing approximately 0.2% of all fractures, and are generally associated with fractures of the tarsal and metatarsal bones.[6]

Although fracture of the cuneiform bones is common, the most common fracture in the tarsometatarsal complex occurs at the base of the second metatarsal. Fractures of the navicular, cuboid, and other metatarsals are less common.[7-10]

The literature indicates that the vast majority (87.5%) of these injuries are closed, and that up to one-third of these injuries occur in athletes during low-energy sports trauma.[11,12]

All the authors declare that there is no potential conflict of interest referring to this article.

Study conducted at Universidade de São Paulo, Faculdade de Medicina, Department of Orthopedics and Traumatology, Laboratório de Investigação Médica do Sistema Musculoesquelético, São Paulo, SP, Brazil.
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Two trauma mechanisms are described: high and low energy. High-energy injuries may result from direct or indirect trauma. Application of a direct load to the dorsal surface of the joint complex, which occurs from crushing or the impact of an object on the static foot, may result in injuries to the bones or to the ligaments through the joint line. The pattern may vary depending on where the force is applied. This type of injury can cause significant damage to the soft tissues, compromising the treatment sequence.[13-15] However, the most common mechanism is indirect injury, which is characterized by a longitudinal force on one foot in plantar flexion. Bone injuries and more severe instabilities usually result from high-energy trauma such as falls from heights or car crashes. The injuries may be evident, but in a considerable portion of patients, spontaneous reduction may occur after the trauma, thus masking the underlying instability. Low-energy injuries include sports traumas, for example in American football.[2,14,16-18] The diagnosis is made by evaluating anteroposterior, lateral, and oblique X-rays of the foot bearing weight. It is important to stress that weight bearing X-rays be done, because in some cases, as mentioned previously, the instability will only be evident after load is placed on the feet.[14,19] The most common finding is diastasis between the base of the first and second metatarsals. Any fracture of the first three metatarsals increases suspicion of the existence of a Lisfranc injury. Computed tomography plays an important role in diagnosis by detecting small fractures and deviations and identifying possible associated injuries.[7,20]

One of the classifications used most commonly in assessing Lisfranc injuries is that of Quenu and Kuss,[21] which divides Lisfranc injuries into types A, B, and C. Type A involves homolateral rupture, in which all metatarsals move in the same direction. In type B injuries, there is an isolated rupture which can involve the first metatarsal or the smaller rays. Type C is divergent displacement, where the first ray and lesser rays are dislocated in opposite directions.

To define the treatment for a Lisfranc injury, assessment of joint stability is essential. Unstable injuries require surgical treatment with anatomical reduction and stable fixation.

It should be emphasized that many patients with injuries restricted to the ligaments develop chronic pain and instability, although anatomical reduction and stable fixation are achieved.[22,23]

The most frequent acute complications are acute compartmental syndrome, vascular damage, skin necrosis, and superficial infections.[24]

The objective of this study was to investigate the epidemiology of Lisfranc injuries found in hospitalized patients.

MATERIALS AND METHODS

The study was approved by the Institutional Review Board under process number 924 and the record CAPpesq/HC 9335.

All medical records for patients hospitalized with foot and ankle fractures between January 2006 and December 2010 were analyzed. Review of these records identified 42 cases of Lisfranc injuries. The parameters analyzed were age, gender, laterality, exposure, injury mechanism, fracture type, classification, associated injuries, emergency treatment, definitive treatment, time between trauma and definitive treatment, length of hospital stay, and acute post-operative complications.

RESULTS

Among the 42 patients studied, we observed that these injuries occurred predominantly in men, who accounted for 81% of the patients. The mean age of the patients studied was 35.5 years, ranging from 19 to 66 years. (Figure 1) The left side was more frequently affected, corresponding to 24 patients, or 57% of the cases.

The most common injury mechanism was automobile accidents in 35.8% of cases, followed by motorcycle accidents (33.3%), falls from height (23.0%), and sports accidents (7.7%). (Figure 2) Of the total, seven (16.7%) patients experienced multiple traumas.

Of the 42 cases, 35 presented closed injuries and 7 had open injuries (16.7%).

According to the classification of Quenu and Kuss, 43% of the patients presented homolateral injuries (type A), 50% had isolated injuries (type B), and 7% had divergent injuries (type C).

Seventy-eight percent of the patients had fractures associated with an injury to the Lisfranc complex. The most prevalent associated fracture was of the second metatarsal, which was present in 16 of the 42 individuals studied (38%). The third metatarsal was involved in 14 cases (33%), followed by the fourth metatarsal in 9 cases (21%). Other associated fractures were of the cuboid bone in 11 cases (26%), the navicular bone in 10 cases (24%), the cuneiforms in seven cases (17%), the tibia diaphysis in six cases (14%), and malleolar fractures in five cases (12%). (Figures 3 and 4).

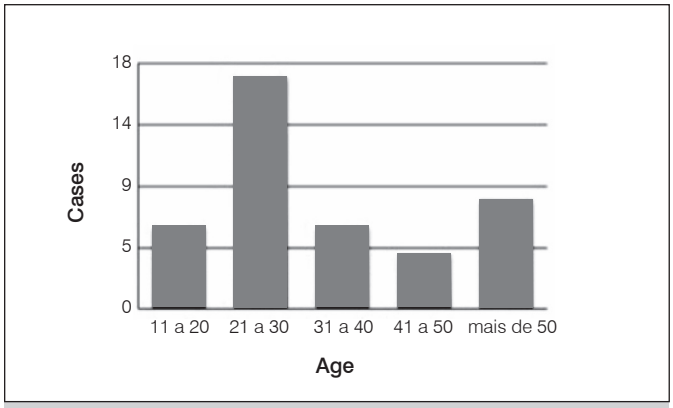

Figure 1. Age range.

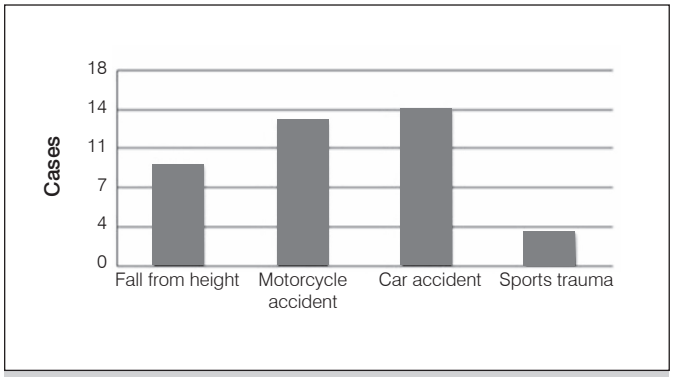

Figure 2. Injury mechanism.

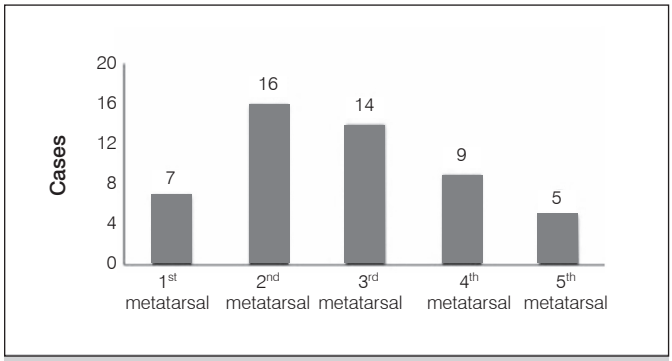

Figure 3. Fractured metatarsal.

Of the 42 patients studied, in five cases conservative treatment was chosen. Of the 37 cases treated surgically, primary arthrodesis was performed in two patients, and reduction and internal fixation were performed in the remaining 35. In relation to fixation method, in 21 cases cannulated screws alone or associated with Kirschner wires were used, eight cases were treated with only Kirschner wires, and plates were used in six cases. Two cases required an external mini-fixator to maintain length.

The average length of time between the temporary treatment and definitive fixation was 6.7 days, varying from 0 to 28 days.

In terms of acute complications, we observed 6 cases of post-operative infection (14%). Of these, one case required a microsurgical flap to cover the wound. One case of superficial skin dehiscence occurred, one case of deep venous thrombosis.

The median hospital stay was 13.8 days, ranging from 0 to 55 days. (Figure 5)

DISCUSSION

This present study was conducted over a period of four years (2006 to 2010) in a tertiary hospital specializing in orthopedics and traumatology which treats a significant number of emergency cases.

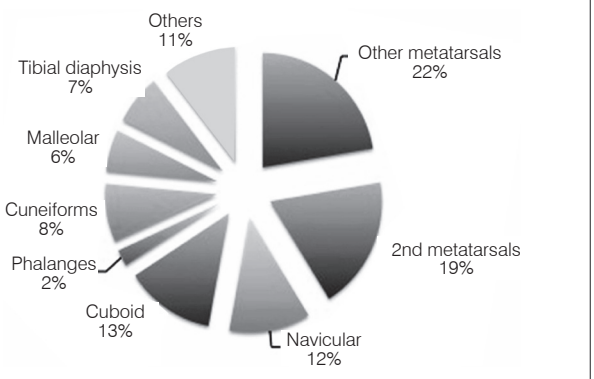

Figure 4. Associated fractures.

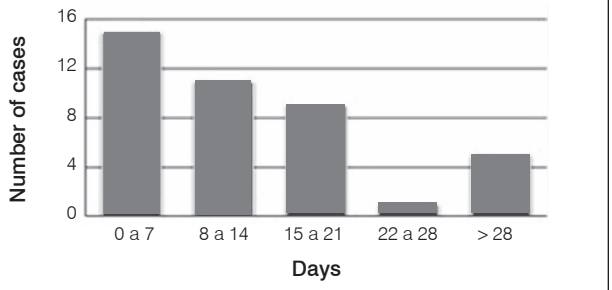

Figure 5. Duration of hospitalization.

It is consequently noted that Lisfranc injury has a low prevalence in the universe of surgically-treated fractures, with a mean frequency of 10.5 cases per year in this service.

We note that, in our study, this type of injury predominantly affected men (81%) and average patient age was 35.5 years. This is a young and economically active population which is affected by significant financial and social losses from this type of injury. In epidemiological terms, it is compatible with the literature, which reports greater incidence of this injury around 30 years of age and 75% predominance in men.[7,25]

Motor vehicle accidents accounted for 69% of the total trauma mechanisms, with auto accidents slightly more common than motorcycle accidents. However, sports accidents corresponded to only 7.7%, a lower prevalence than suggested by the literature. Benirschke et al.[12] showed in their study that this type of mechanism could account for up to 30% of cases. This discrepancy may be attributed to the different epidemiological profile of the patients treated at our institution. Since the Hospital das Clínicas is a reference hospital, there is a predominance of high-energy trauma such as auto and motorcycle accidents.

The left side was more affected (57%) and open fractures were present in 17% of cases. This rate is in accordance with the international literature. According to Stavlas and Miswan, the prevalence of open fractures in this type of injury may vary from 12.5 to 26%.[11,25]

In 33 cases (78.6%), associated fractures were present, similar to the findings by Aitken et al.[26] and Meyerson et al.,[2] who also observed a higher frequency of fractures at the base of the second metatarsal and the cuboid bone.

In only five cases (12%) was conservative treatment chosen, which demonstrates the predominance of surgical treatment of this type of injury. Definitive surgical treatment occurred an average of six days after the initial trauma. Definitive treatment for Lisfranc injuries can be postponed in situations with large soft tissue injuries, acute compartment syndrome, and open fractures secondary to crushing. Consequently, there is no consensus in the literature with regard to the ideal period for conducting the definitive procedure.[24]

As for acute complications associated with fracture or treatment, the post-operative infection rate in our study was 14.3%, higher than that reported in the literature, which ranges from 4.8% to 7.3%.[27,28] One case of post-operative infection progressed and required a microsurgical flap for coverage. Only one patient developed deep venous thrombosis.

The mean hospital stay was 13.8 days. This lengthy average hospitalization can be primarily attributed to the patients with multiple traumas whose definitive treatments were delayed, as well as to acute post-operative complications such as infections and complications of the surgical wound. This prolonged period of hospitalization generates high costs for the public health system and also lowers bed turnover.

CONCLUSION

Although rare, Lisfranc injuries found in patients hospitalized in a high-complexity service occurred in young men who were involved in motor vehicle accidents, and most cases involved an associated fracture of another bone in the foot. The incidence of acute complications is high and hospital stays are lengthy.

AUTHORS' CONTRIBUTIONS: Each author contributed individually and made significant contributions to the development of this manuscript. MFS (0000-0002-0643-9538)* and GHS (0000- 0002-1211-9258)* collected the data from the patient records and conducted the bibliographic research, evaluated and interpreted the data collected, and drafted the manuscript. PAP (0000-0001-9667-0006)* collected data from the patient records. MHS (0000-0001-7969-0515)* analyzed the data collected, and drafted and revised the manuscript. MHS, PAP, ALGS (0000-0002-6672-1869),* and PTO (0000-0002-9687-7143)* performed the final revision of the manuscript, and also contributed to the intellectual concept of the study. *ORCID (Open Researcher and Contributor ID)..

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ORIGINAL ARTICLE

BIMALLEOLAR ANKLE FRACTURE: A SIMPLE FRACTURE?

FRATURA BIMALEOLAR DO TORNOZELO: UMA SIMPLES FRATURA?

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ABSTRACT

Objective: To evaluate the frequency of deltoid ligament injury in bimalleolar supination-external rotation type fractures and whether there is a correlation between the size of the fractured medial malleolus and deltoid ligament injury. Methods: Twenty six consecutive patients underwent magnetic resonance exams after clinical and radiographic diagnosis of bimalleolar supination-external rotation type ankle fractures. Results: Thirteen patients (50%) presented deltoid ligament injury associated to bimalleolar ankle fracture. Partial injury was present in seven (26.9%) patients and total injury in six (23.1%). Regarding medial fragment size, the average was 2.88 cm in the absence of deltoid ligament injury. Partial injuries presented 1.93 cm and total 2.1 cm on average. Conclusion: Deltoid ligament injury was present in 50% of bimalleolar ankle fractures. Smaller medial malleolus fragments, especially concerning the anterior colliculus, presented greater association with partial deltoid ligament injuries. ***Level of Evidence IV, Cross Sectional Study.***

Keywords: Ankle. Ankle fractures. Ligaments. Magnetic resonance imaging.

RESUMO

Objetivo: Avaliar a frequência da lesão do ligamento deltóide nas fraturas bimaleolares do tornozelo tipo supinação-rotação externa e se existe correlação entre o tamanho do fragmento do maléolo medial fraturado e o tipo de lesão do ligamento deltóide. Métodos: Vinte e seis pacientes consecutivos com diagnóstico clínico e radiográfico de fratura bimaleolar do tornozelo tipo supinação-rotação externa (Lauge-Hansen), foram submetidos ao exame de ressonância magnética do tornozelo para avaliar a presença de lesão ligamentar associada à fratura bimaleolar. Resultados: Treze pacientes (50%) apresentaram lesão do ligamento deltóide associada à fratura bimaleolar do tornozelo, sendo sete (26,9%) lesões parciais e seis (23,1%) totais. Com relação ao tamanho do fragmento do maléolo medial, na ausência de lesão do ligamento deltóide, o tamanho médio foi de 2,88 cm. Nas lesões parciais, a média foi de 1,93 cm e, nas lesões totais do ligamento deltóide, de 2,1 cm. Conclusões: A lesão do ligamento deltóide esteve presente em metade das fraturas bimaleolares do tornozelo do tipo supinação-rotação externa. Fragmentos menores do maléolo medial, especialmente do colículo anterior, tem maior associação com lesões parciais do ligamento deltóide. ***Nível de Evidência IV, Estudo Transversal.***

Descritores: *Tornozelo. Fraturas do tornozelo. Ligamentos. Imagem por ressonância magnética.*

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INTRODUCTION

Ankle fractures are among the most common injuries treated by orthopedic surgeons.

Typically, ankle fractures result from low-energy rotational traumas. But as numbers of traffic accidents have increased, the severity of the fractures and trauma energy have grown steadily.[1-5]

Stability of the ankle joint is provided by the medial and lateral malleoli and their respective ligaments.

Careful identification of these injuries and their treatments involve not only recognition of bone injuries, but also identification of damage to the soft tissue and ligaments.

Tornetta[6] described the importance of assessing the ankle joint through traditional x-ray parameters and stated that the ankle joint must not be assessed as only a bony component, but rather an osteoligamentous joint surrounded by soft tissue. These lateral and medial ligament complexes have an important relationship with the pathophysiology of ankle fractures and with the therapeutic approach.

The deltoid ligament is the primary stabilizer of the ankle. Its superficial and deep tracts can rupture as a result of rotational trauma, leading to instability and chronic pain in this joint.[7]

The authors of this study hypothesize that magnetic resonance imaging (MRI) can provide important information for identifying ligament injuries associated with bimalleolar fractures of the ankle joint such as supination-external rotation according to the Lauge-Hansen classification.

All the authors declare that there is no potential conflict of interest referring to this article.

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The aim of this study was to obtain MRI from patients with supination-external rotation type bimalleolar ankle fractures in order to assess the frequency of concomitant deltoid ligament injuries and the relationship between the size of the fractured medial malleolus fragment and the type of injury to the deltoid ligament.

METHODS

The present study was approved by the Institutional Review Board of the main institution under the number 15632813.9.0000.5149 and was conducted in accordance with the standards of the Helsinki Declaration.
The sample consisted of 26 consecutive patients treated at a general hospital with a clinical and radiographic diagnosis of bimalleolar fracture of the ankle, Lauge-Hansen supination-external type; MR imaging (using a Philips Intera 1.5 tesla device) was obtained for the affected joint.
The resulting imaging was analyzed by a radiologist specializing in MRI and a member of the Brazilian College of Radiology, as well as a physician belonging to the Brazilian Society of Orthopedics and Traumatology and the Brazilian Society of Orthopedic Trauma.
The inclusion criteria were: adult patients (17 years or older) with supination-external rotation type bimalleolar fracture of the ankle who read and signed the terms of free and informed consent and agreed to be included in the study.
The exclusion criteria were: skeletally immature patients, patients who refused to sign the terms of consent, and patients with other ankle fracture patterns than those mentioned in the inclusion criteria.
Sample: Of the 26 patients, 16 (61.54%) were male and 10 (38.46%) were female. Eleven patients (42.32%) had trauma on the left side and 15 (57.69%) on the right side.
The type of trauma was car accident in six patients (23.1%), pedestrian hit by a vehicle in two patients (7.7%), fall from height in four patients (15.4%), trip-and-fall in 13 patients (50%), and sports trauma in one patient (3.8%).
Patient age ranged from 19 to 50 years, with a mean of 32.3.
A descriptive analysis was performed of the data and 95% confidence intervals (CI) were constructed for the proportions sex, side, presence of injury to the deltoid ligament, presence of total deltoid ligament rupture, and presence of partial deltoid ligament rupture. Since the sample size was less than 30 and the central limit theorem could not be used, we used exact calculation of the confidence interval based on binomial distribution, the interval of which is generally not symmetrical in relation to the estimated proportion. We also constructed 95% confidence intervals for the mean age and mean size of the fragment of the medial malleolus. To calculate this latter interval, because the sample was smaller than 30 and the central limit theorem again could not be used, we tested the adhesion of the variables age and size of the fragment of the medial malleolus and normal distribution using the Anderson Darling test.[8]
Non-parametric analysis of variance was conducted using the Kruskal-Wallis test to test at a 5% significance level whether the size of the fragment of the medial malleolus is identical in all three groups (no injury to the deltoid ligament, partial rupture of the deltoid ligament, and total rupture of the deltoid ligament), making contrasts by pairs to detect which differences were significant.[9]
The hypothesis that the average size of the medial malleolus fragment in patients with total ligament rupture was no greater than 2.8 cm was also tested against the alternative hypothesis that the fragment in this group was greater than 2.8 cm at 5% significance using the non-parametric Wilcoxon signed-rank test. We also tested the hypothesis that the average size of the medial malleolus fragment in patients with partial ligament injury was at least 1.7 cm against the alternative hypothesis that the fragment was smaller than 1.7 cm, according to the parameters standardized by Tornetta.[6]
Since the hypothesis tests were performed at a 5% significance level, hypotheses with descriptive levels below 0.05 were also discarded.

RESULTS

Thirteen patients (50%) exhibited injury to the deltoid ligament (CI=[29.93; 70.07]%), seven (26.9%) had partial rupture of this ligament (CI =[11.57; 47.79]%), and seven (23.1%) had total rupture of this ligament (CI = [8.97; 36.07]%).
The size of the fragment of the medial malleolus ranged from 1.6 cm to 3.3 cm with a mean of 2.6 cm and standard error of 0.101 cm. We tested adherence to the size distribution of the medial malleolus fragment to the normal distribution, and this hypothesis was not rejected (P = 0.061). Consequently, the CI for the medial malleolus fragment was [2.362; 2.777] cm.
Figure 1 illustrates the magnetic resonance imaging for two patients with fractures of the medial malleolus.
The Kruskal-Wallis test was used to evaluate the hypothesis that the size of the medial malleolus fragment was identical in all three groups (no injury to the deltoid ligament, partial rupture of the deltoid ligament, and total rupture of the deltoid ligament), and this hypothesis was rejected (P = 0.001). Contrasts showed at 5% significance that the size of the medial malleolus fragment differs (is smaller) when the rupture is partial when compared to the respective fragment sizes and other injury types (total rupture, no injury). It was also concluded that there was no significant difference in the size of the medial malleolus fragment when there was no injury to the deltoid ligament and when a total rupture was present.
Table 1 and Figure 2 present the results.
The non-parametric Wilcoxon signed-rank test at 5% significance was used to test the hypothesis that the mean size of the medial malleolus fragment in patients with total ligament rupture was no more than 2.8 cm, and this hypothesis was not rejected (P = 0.799).
The hypothesis that the mean medial malleolus fragment with partial ligament rupture was at least 1.7 cm was also tested at 5% significance, and this hypothesis was also not rejected (P = 0.929).

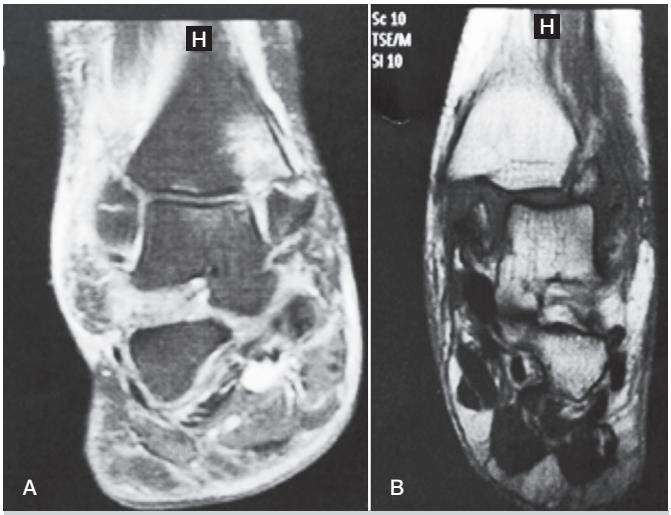


Figure 1. (A) Magnetic resonance imaging of the ankle in coronal plane showing a Weber B fracture, supination-external rotation stage 4, with fragment of the medial malleolus containing a small deviation and integrity of the deltoid ligament. (B) Magnetic resonance imaging of the ankle in coronal plane showing a Weber B fracture, supination-external rotation stage 4, with medial malleolus fragment 2.3 cm in size and total rupture of the deltoid ligament.

Table 1. Measurements of medial malleolus fragment (in cm), mean, and standard error (SE).

Injury	Absent	Partial	Total
	2.9	1.6	2.3
	2.8	2.6	3.3
	3.2	1.8	2.5
	2.9	1.6	2.6
	2.9	2.3	3.1
	2.7	1.7	2.1
	2.6	1.9	
	2.8		
	3.2		
	2.6		
	2.7		
	3.1		
	3.0		
Mean	2.88	1.93	2.65
SE	0.06	0.14	0.19

SE: Standard Error

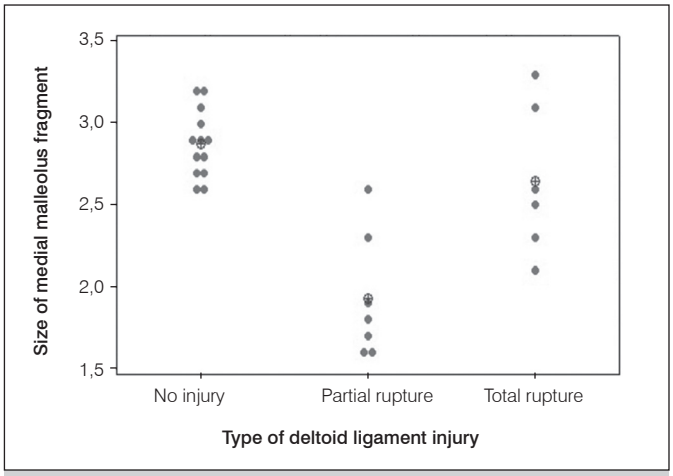


Figure 2. Graph of individual values for medial malleolus fragment size and mean (circle with a cross) for each group.

DISCUSSION

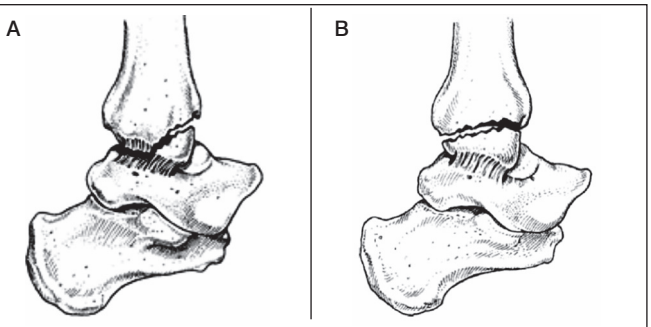
Fractures classified by Lauge-Hansen as supination-external rotation type are the most prevalent malleolar fractures, accounting for 40-75% of ankle fractures.[4,5,10] In this fracture pattern, the injury begins in the lateral component, and may progress to the medial side depending on the energy of the trauma. The fourth stage of the injury involves the deltoid ligament and/or fracture of the medial malleolus.

The superficial deltoid ligament, which originates in the anterior colliculus, does not contribute greatly to ankle stability.[11]

Recently, the ligament injuries associated with anterior colliculus fracture of the medial malleolus have been described.[6,11-17] In this pattern of medial malleolus fracture, we find fracture of the anterior colliculus with the posterior colliculus intact. This allows the energy to pass through the posterior portion of the deltoid ligament and causes a partial rupture in this ligament. (Figure 3)

Therefore, the size of the medial fragment injury is intimately linked to the competence and integrity of the deltoid ligament. Tornetta[6] found that fractures of the medial malleolus greater than 2.8 cm in length (supracollicular fractures) have intact ligaments, while malleolar fractures smaller than 1.7 cm (fracture of the anterior colliculus or intercollicular fractures) compromise the competence of the deltoid ligament.

In the present study, seven patients presented partial rupture of the deltoid ligament, predominantly involving the deep portion. These data resemble the findings by Tornetta,[6] who found 26% incompetence of the deltoid ligament.



Adapted from: Tornetta P 3rd. Competence of the deltoid ligament in bimalleolar ankle fractures after medial malleolar fixation. J Bone Joint Surg Am 2000;82:843-8.

Figure 3. (A) anterior colliculus fracture with small fragment and continuous injury of the deep fibers of the deltoid ligament (partial tear: posterior and deep portion); (B) medial malleolus fracture with the fracture line passing through all the collicular surfaces, causing medial instability in the ankle but without injury to the deltoid ligament.

Based on the data presented regarding the average size of the medial malleolus fragment and injury to the deltoid ligament demonstrated in the MRI, we found a relationship between the size of the medial malleolus fragment and the rupture of the deltoid ligament. This analysis found similar average values in relation to the size of the medial malleolus fragment, and showed that fractures with larger fragments also tended to feature an intact deltoid ligament. Fractures with smaller fragments of the medial malleolus showed partial rupture of the deltoid ligament with integrity in the superficial portion (usually still inserted in the anterior colliculus) and rupture of the deep portion. Total rupture of the deltoid ligament was found in patients with bone fragments with an average size of 2.6 cm.

Limitations of this study include a relatively small sample size (26 patients), lack of pre- and post-hoc power analysis, and lack of correlation between the presence of deltoid ligament injury associated with bimalleolar fracture and treatment or prognosis. MRI is still a relatively expensive examination and is not available for most emergency medical services in developing countries.

Among the positive points of this study, the authors confirmed the hypothesis that MRI is valuable in diagnosing ligament injuries of the ankle associated with bimalleolar fractures, confirming the findings by Tornetta.[6] It is essential to stress the importance of early identification of injuries to the deltoid ligament concomitant with ankle fractures, an injury that seems to be more frequent than previously thought. The authors were unable to find any studies in Portuguese published at the time of this writing demonstrating this common association.

CONCLUSION

In Lauge-Hansen type supination-external rotation bimalleolar fractures of the ankle, the deltoid ligament was also ruptured in half of cases. When the deltoid ligament rupture was partial, the medial malleolus fragment was smaller (fracture only in the anterior colliculus) than when the ligament was completely ruptured or when there was no injury.

There was no significant difference in the size of the medial malleolus fragment when there was no injury to the deltoid ligament and when the rupture was total.

Future studies with more meaningful sample sizes and a cost-benefit analysis of introducing MRI into the diagnostic arsenal of emergency services for ankle fractures are needed to validate the hypothesis that bimalleolar fractures, which are considered relatively easy to treat, may present associated ligament injuries that can lead to instability and chronic pain in the ankle if not treated properly.

AUTHOR CONTRIBUTIONS: Each author made individual and significant contributions to the development of this manuscript. JMF (0000-0003-4865-4866)* and RESP (0000-0002-3572-5576)* were the main contributors to the writing of the manuscript. JMF, JOSH (0000-0003-2215-9103)*, and RLD (0000-0002-4441-6679)* attended the patients, requested MRIs, and analyzed the results. JMF, RESP, and PJL (0000-0003-4967-7576)* evaluated the data from the statistical analysis. JMF, RESP, PJL, JOSH, and RLD conducted the literature search and reviewed the manuscript. All authors contributed to the intellectual concept of the study. *ORCID (Open Researcher and Contributor ID).

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DIAGNOSIS AND TREATMENT OF POSTERIOR INTEROSSEOUS NERVE ENTRAPMENT: SYSTEMATIC REVIEW

DIAGNÓSTICO E TRATAMENTO DAS COMPRESSÕES DO NERVO INTERÓSSEO POSTERIOR: REVISÃO SISTEMÁTICA

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ABSTRACT

Compressive syndromes of the radial nerve have different presentations. There is no consensus on diagnostic and therapeutic methods. The aim of this review is to summarize such methods. Eletronic searches related terms, held in databases (1980-2016): Pubmed (via Medline), Lilacs (via Scielo) and Google Scholar. Through pre-defined protocol, we identified relevant studies. We excluded case reports. Aspects of diagnosis and treatment were synthesized for analysis and tables. Quantitative analyzes were followed by their dispersion variables. Fourteen studies were included. All studies were considered as level IV evidence. Most studies consider aspects of clinical history and provocative maneuvers. There is no consensus on the use of electromyography, and methods are heterogeneous. Studies have shown that surgical treatment (muscle release and neurolysis) has variable success rate, ranging from 20 to 96.5%. Some studies applied self reported scores, though the heterogeneity of the population does not allow inferential analyzes on the subject. few complications reported. Most studies consider the diagnosis of compressive radial nerve syndromes essentially clinical. The most common treatment was combined muscle release and neurolysis, with heterogeneous results. There is a need for comparative studies. ***Level of Evidence III, Systematic Review.***

Keywords: Radial nerve. Nerve compression syndromes/diagnosis. Nerve compression syndromes/therapy. Evidence-based medicine.

RESUMO

As síndromes compressivas do nervo radial tem apresentação diversa. Não há consenso sobre métodos diagnósticos e terapêuticos. O objetivo desta revisão é sintetizar tais métodos. Este estudo se baseou no método das revisões sistemáticas da literatura. Busca eletrônica de estudos primários utilizando termos correlatos, realizada nas bases de dados (1980 a 2016): Pubmed (via medline), Lilacs (via Scielo) e Google Scholar. Através de protocolo pré-definido, identificou-se estudos relevantes. Não houve restrições de idioma. Excluiu-se relatos de caso. Aspectos do diagnóstico e tratamento foram sintetizados em tabelas. Análises quantitativas foram seguidas de suas variáveis de dispersão, considerando IC de 95%. Incluiu-se catorze estudos foram incluídos. Todos estudos foram considerados como nível IV de evidência. A maioria dos estudos consideram aspectos da história clínica e manobras provocativas como definidores de diagnóstico. Não há consenso sobre utilização da eletroneuromiografia, e os métodos são heterogêneos. Estudos demonstram que o tratamento cirúrgico (liberação muscular e neurólise) apresenta taxa variável de bons resultados, variando de 20-96,5%. Alguns estudos aplicaram escores autorreportados, entretanto a heterogeneidade das populações não permite análises inferenciais sobre o tema. Reportou-se poucas complicações. A maioria dos estudos consideram o diagnóstico da síndromes compressivas do nervo radial eminentemente clínicas. O tratamento cirurgico mais utilizado foi técnica mista de liberação muscular e neurólise, com resultados heterogêneos. Necessita-se de estudos comparativos. ***Nível de Evidência III, Revisão Sistemática.***

Descritores: *Nervo radial. Síndromes de compressão nervosa/diagnóstico. síndromes nervosas compressivas/terapia. Medicina baseada em evidências.*

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INTRODUCTION

Compressive syndromes of the radial nerve present themselves in distinct ways; they can be purely sensory, motor or mixed.[1] This group contains several syndromes such as radial tunnel syndrome, Wartenberg's syndrome, and posterior interosseous nerve syndrome. Because these syndromes affect different compression sites, they present distinct clinical conditions and potential diagnostic intersection with other conditions such as lateral epicondylitis of the elbow. The most common compressive syndromes are distal to the level of the elbow.[1,2]

All the authors declare that there is no potential conflict of interest referring to this article.

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Methods for diagnosing these injuries are based on clinical criteria but may also include imaging methods and electrophysiological studies.[2] These diagnostic criteria vary widely because of both clinical maneuvers and quantitative criteria of imaging examinations.[2] This fact makes the study of this group of diseases challenging because there is a lack of uniformity. Along similar lines, controversy exists with regard to treatment methods (conservative versus surgical) and there is no criteria for defining good or bad results.

Systematic literature reviews are secondary studies (utilizing research from primary studies) that bring together and synthesize data in order to summarize the stage of research on a given topic, standardize the current research, and propose strategies for future studies.[3] This is an essential function to advance research on the topic, in addition to guiding those who are interested in the field.[4] Using a systematic review, the objective of this study was to describe the clinical conditions (in adult patients), diagnosis, and treatment of compressive syndromes of the radial nerve, more specifically posterior interosseous nerve syndrome while excluding traumatic conditions and open injuries such as paralysis after humeral fracture.

METHODS

The presentation of this systematic review follows the parameters of the PRISMA Statement,[5] which regulates the methods of dissemination for systematic reviews and meta-analyses. This study was approved by the Institutional Review Board of the Universidade Federal de São Paulo under process number CEP 0108/2016.

The selected clinical studies were from adult patients with radial nerve entrapment syndromes, which aimed to present results of diagnosis and treatment. Studies conducted since 01/01/1980 were included, and there were no restrictions on language or with regard to follow-up time or temporality of the study (prospective/retrospective review). The following study designs were included: case series (retrospective/prospective study), case-control, cohort studies, and randomized clinical trials. We opted to exclude case reports.

The data were obtained from the Pubmed database (via Medline, searched in March 2015), the Lilacs database (via Scielo, searched in March 2016) and Google Scholar, using an active keyword search (MesH and non-MesH): Search terms were (Medline via Pubmed, Scielo, and Google Scholar): "radial tunnel syndrome" AND "radial neuropathy" AND "radial nerve palsy" AND "radial nerve neuritis" AND "posterior interosseous nerve neuropathy" AND "radial nerve neuropathy" AND "radial nerve palsy" and free search for the terms "radial nerve compression", "radial nerve syndrome", "Wartenberg syndrome", "radial nerve entrapment", "posterior interosseous compression". The operator OR was used for combinations of the terms in Pubmed. For Lilacs, an end-to-end study was used, and was limited to 01/01/1980. For relevant studies, we determined we would contact the study authors if there were any difficulties obtaining the data.

The studies were selected by assessing the title and structured abstract after selection in duplicate by two researchers (MM and RG). When there was disagreement between the researchers, a third researcher cast the tie-breaking vote (VM).

Data extraction

The data were extracted using a protocol which was defined *a priori* and comprised the following information: description of the disease/condition, author, year of publication, journal, type of study, participants (inclusion and exclusion criteria), diagnostic criteria (criteria for clinical diagnosis, diagnostic criteria for supplementary examinations), intervention (clinical, surgical), results (symptoms cured/functional scores) and complications.

Statistical analysis

After obtaining the data provided in this form, the authors gathered to summarize the data using qualitative tables (description of the condition, diagnostic methods, treatment methods, inclusion and exclusion criteria) and quantitative analysis via meta-analysis (risk/relative risk ratio and/or difference between the means). We chose to use REVMAN version 5.0 software for the quantitative analysis; the quantitative data were followed by their 95% confidence intervals. We chose to use a 5% alpha in the inferential analyses. The heterogeneity among the studies was assessed using I^2, and heterogeneity was considered high if I^2 was greater than 75%.

RESULTS

We found 14 studies addressing the topic of this review.[6-19] The flow chart (Figure 1) indicates the steps we took to obtain the included studies.

The demographic characteristics and the bibliometrics of the studies are presented in Tables 1 and 2.

In most studies, the clinical criteria were standardized, and some studies included eletroneuromyographic criteria. The majority included semiological aspects (principally pain) and semio-technical aspects (challenge via clinical maneuvers).

The results of the treatment, which for the most part are displayed qualitatively without focus on qualitative variables, showed high heterogeneity among the studies, with a discrepancy varying from 39 to 100% good results.

The proportions and confidence intervals, calculated for the purpose of this review, are shown in Table 3. Quantitative data were present in some studies,[10,11,14,15,17,18] and utilized the self-reported DASH/QuickDash and Roles & Maudsley tools. In general, the majority of studies described the open technique with muscle release associated with external neurolysis in the radial nerve. The exception that should be noted is the study by Lèclere et al.,[11] who treated patients endoscopically.

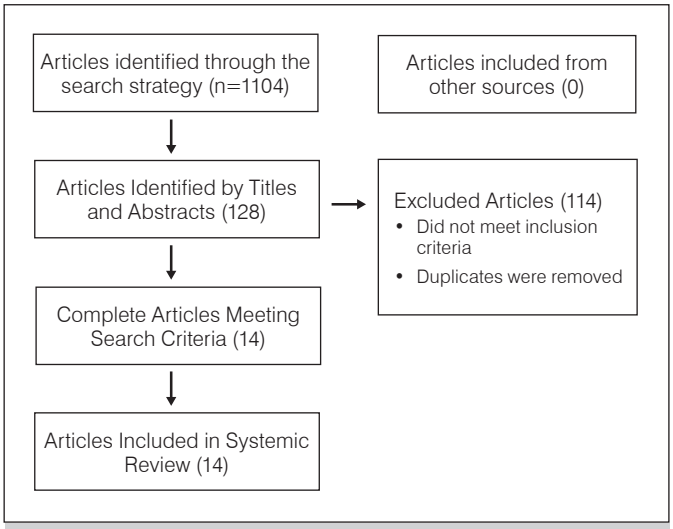

Figure 1. Flowchart of the search for studies.

Table 1. Characteristics of the included studies.

	Mean	Standard Deviation
Number of participants (n=14)	34.57	28.5
The number of limbs receiving intervention (n=14)	34.85	29.6
Time of follow-up (n=12)	86.08	72.8
Lost to follow-up (n=3)	7.3	2.5

Table 2. Characteristics of the studies: quantitative data.

Origin (n; %)	Type of journal (n; %)	Type of study (n; %)
Europe (7; 50%)	Hand surgery (3; 21.4%)	Case series, retrospective (7; 46.7%)
Asia (2; 14.2%)	Ortopedia (6; 42,8%)	Séries de caso, prospectiva (5; 33,4%)
Americas (5; 35.8%)	Electrophysiology (1; 7.1%)	Case series, prospective (5; 33.4%)
	Outras (4;28,5%)	Comparative study (case-control) (2; 3.4%)
	Other (4; 28.5%)	

Table 3. Characteristics of the studies: quantitative data.

Study	Proportion of good results	Confidence Interval
Hashizumi, 1996[9]	93%	n/a
Jebson, 1997[10]	48%	31%-65.5%
Leclère, 2012[11]	100%	n/a
Quignon, 2011[14]	60%	35.2%-84.8%
Rinker, 2004[15]	94%	n/a
Perez, 2014[17]	86%	75.7%-96.4%
Sotereanos, 1999[18]	39%	21.2%-75.4%

DISCUSSION

In the absence of conclusive and well-delineated studies, the systematic reviews of non-randomized studies presented the following benefits: 1) they map the status of evidence, which is often deficient; 2) they determine failures in the process of determining scientific truths about the topic; 3) they quantify the available evidence, and 4) they propose and expose opportunities for future research, affirming the mobilization of human efforts and financial resources. The results of this review demonstrated the poor quality of evidence on the subject. For the most part the studies were level IV evidence, susceptible to bias from memory and selection, and as a rule they tended to overestimate the effects of treatment and bias the sample of patients. Consequently, the results of this review are limited, but they do serve to illustrate the current state of research, ratifying and supporting new studies on the theme.

The results show that there is no uniformity in diagnosis and treatment, but the clinical criteria and treatment remained constant in some studies. In this respect, studies of accuracy (diagnostic properties of clinical maneuvers, electroneuromyography, and imaging examinations and comparison of treatment methods such as isolated muscle release, individual occurrence or association with neurolysis, and endoscopic methods) are a prolific area for science. This should, however, counterbalance the difficulty of grouping cohorts on this topic, because of its relatively low frequency and low rate of diagnosis.

Despite this lower frequency, the studies show a considerable rate of good results, but extrapolation of these results to practice can be subject to reference bias since the evaluator is not blinded, and there is no effective methodology for measuring outcomes, which should focus on patient-reported outcomes and measures of pain and recurrence. The literature exhibits a lack of studies reporting conservative treatment techniques, which leads us to raise the possibility that the cohorts in these studies are for the most part patients refractory to conservative methods of treatment. The small rate of complications, which could be the result of underreporting, should also be mentioned.

FINAL CONSIDERATIONS

We found that the majority of studies consider diagnosis of compressive syndromes of the radial nerve to be eminently clinical. The most common treatment consisted of a mixed technique of muscle release and external neurolysis, with heterogeneous results. There is a need for comparative studies on the subject, ideally multi-center studies which examine the effectiveness of treatment methods and pay special attention to conservative methods of treatment.

AUTHOR CONTRIBUTIONS: Each author contributed individually and made significant contributions to the development of this manuscript. VYM (0000-0002-4933-4007)*, MAM (0000-0002-8165-115X)*, and RGG (0000-0002-2876-1210)* were the main contributors in the drafting of the manuscript, conducting the literature reviews, evaluating the data from the statistical analysis, and revising the manuscript. VYM, JBGS (0000-0003-4134-2093)*, JCB (0000-0003-3396-479X)* and FF(0000-0003-3688-8729)* contributed to the intellectual concept of the study. *ORCID (Open Researcher and Contributor ID)

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A nimesulida não deve ser administrada durante a gravidez ou em mulheres que estejam amamentando.** CUIDADOS E ADVERTÊNCIAS: Paramente nimesulida foi relatada estar associada com reações hepáticas sérias, incluindo casos fatais. Pacientes que apresentaram sintomas compatíveis com dano hepático durante o tratamento com nimesulida (por exemplo, anorexia, náusea, vômitos, dor abdominal, fadiga, urina escura ou icterícia) devem ser cuidadosamente monitorados. A administração concomitante com drogas hepatotóxicas conhecidas e abuso de álcool, devem ser evitados durante o tratamento com nimesulida. Pacientes que apresentaram testes de função hepática anormais devem descontinuar o tratamento e não devem reiniciar o tratamento com a nimesulida. Em raras situações, onde ulcerações ou sangramentos gastrintestinais ocorrem em pacientes tratados com nimesulida, o medicamento deve ser suspenso. Em pacientes com insuficiência renal ou cardíaca, cuidado é requerido, pois o uso de AINES pode resultar em deterioração da função renal. Pacientes idosos são particularmente sensíveis às reações adversas dos AINES, incluindo hemorragia e perfuração gastrintestinal, dano das funções renal, cardíaca e hepática. O uso prolongado de AINES em idosos não é recomendado. A nimesulida deve ser usada com atenção em pacientes com história de ulceração péptica ou inflamações intestinais. Como os AINES podem interferir na função plaquetária, eles devem ser usados com cuidado em pacientes com hemorragia intracraniana e alterações da coagulação, como por exemplo, hemofilia e predisposição a sangramento. As drogas antiinflamatórias não-esteroidais podem mascarar a febre relacionada a uma infecção bacteriana subjacente. Com relação ao uso da nimesulida em crianças, foram relatadas algumas reações graves, incluindo raros casos compatíveis com síndrome de Reye. O uso concomitante de outros anti-inflamatórios não-esteroidais durante a terapia com nimesulida não é recomendado. Como os outros anti-inflamatórios não-esteroidais, a nimesulida deve ser usada com cuidado em pacientes com insuficiência cardíaca congestiva, hipertensão, prejuízo da função renal ou depleção do volume extracelular, que são altamente susceptíveis a uma redução no fluxo sanguíneo renal. Por ser a eliminação do fármaco predominantemente renal, o produto deve ser administrado com cuidado a pacientes com prejuízo da função hepática ou renal. Em pacientes com clearance de creatinina de 30-80 ml/min, não há necessidade de ajuste de dose. Em caso de disfunção renal grave o medicamento é contra-indicado. Em pacientes com história de perturbações oculares devido a outros AINES, o tratamento deve ser suspenso e realizado exames oftalmológicos caso ocorram distúrbios visuais durante o uso da nimesulida. Pacientes com asma toleram bem a nimesulida, mas a possibilidade de precipitação de broncoespasmo não pode ser inteiramente excluída. Os riscos de uso por via de administração não-recomendada são: a não-obtenção do efeito desejado e ocorrência de reações adversas. Atenção diabéticos: contém açúcar (nas apresentações da suspensão oral (900 mg/ml), granulado (1,774 g por envelope) e gotas (300 mg/ml)). GRAVIDEZ E LACTAÇÃO: Categoria de risco de gravidez C: este medicamento não deve ser utilizado por mulheres grávidas sem orientação médica ou do cirurgião-dentista. INTERAÇÕES MEDICAMENTOSAS: A potencial interação com glibenclamida, teofilina, varfarina, digoxina, dimetidina e uma preparação antiácida (ou seja, uma combinação de hidróxido de magnésio e alumínio) foram estudadas in vivo. Nenhuma interação clínica significante foi observada. A nimesulida pode antagonizar os efeitos dos diuréticos e em particular bloquear o aumento da atividade da renina plasmática induzida pela furosemida. O uso concomitante de furosemida e nimesulida requer cautela em pacientes renais ou cardíacos susceptíveis. A administração concomitante de nimesulida com anticoagulantes (varfarina) ou ácido acetilsalicílico pode causar efeitos aditivos (aumento do risco de complicações de sangramento). Portanto, esta combinação não é recomendada e é contra-indicada em pacientes com distúrbios de coagulação graves. Se a combinação não puder ser evitada, a atividade anticoagulante deve ser cuidadosamente monitorada. Se nimesulida for prescrita para um paciente sob terapia com lítio, os níveis de lítio devem ser monitorados cuidadosamente. Deve-se ter cuidado com pacientes que apresentem anormalidades hepáticas, particularmente se houver intenção de administrar nimesulida em combinação com outras drogas potencialmente hepatotóxicas. Não há evidência de que a nimesulida afete a glicemia em jejum ou a tolerância à glicose em pacientes diabéticos tratados com sulfoniluréias. Pode haver potencialização da ação da fenitoína. Embora não tenham sido relatados especificamente com a nimesulida, foram documentadas interações entre antiinflamatórios não-esteroidais e lítio, metotrexato, probenecida e nimesulida. Portanto, recomenda-se cuidado na administração concomitante de nimesulida com qualquer uma destas drogas, devido ao aumento do risco de hemorragias gastrintestinais. Devido ao seu efeito sobre as prostaglandinas renais, os inibidores da prostaglandina-sintetase como a nimesulida podem aumentar a nefrotoxicidade das ciclosporinas. Recomenda-se tomar NISULID após as refeições. Não se aconselha a ingestão de bebidas alcoólicas durante o tratamento. REAÇÕES ADVERSAS: **Pele e tecidos subcutâneos: prurido, rash e sudorese aumentada. Gastrintestinais: diarréia, náusea e vômito. Hepatobiliar: alterações dos parâmetros hepáticos (transaminases), geralmente transitórias e reversíveis. Casos isolados de hepatite aguda, falência hepática fulminante (algumas fatalidades foram relatadas), icterícia e colestase. Sistema nervoso: tonturas e vertigens. Sistemas visual e auditivo: raramente visão borrada. Sistema cardiovascular: hipertensão. Renais: raramente: disúria, hematúria e retenção urinária. Sistema sangüíneo e linfático: raramente: anemia e eosinofilia. Sistema imunológico: raramente hipersensibilidade. Sistema endócrino: raramente hipercalemia. Respiratórios: casos isolados de reações anafiláticas como dispnéia, asma e broncoespasmo, principalmente em pacientes com histórico de alergia ao ácido acetilsalicílico e a outros AINES. Distúrbios gerais: edema.** POSOLOGIA: USO PARA ADULTOS E CRIANÇAS ACIMA DE 12 ANOS. Comprimidos: 50 - 100mg (1/2 a 1 comprimido tomado com 1/2 copo de água) duas vezes ao dia, podendo alcançar até 200 mg duas vezes ao dia. A administração é por via oral. Comprimidos dispersíveis: 100mg (1 comprimido) duas vezes ao dia, podendo alcançar até 200 mg duas vezes ao dia. Dissolver o comprimido em 1/2 copo de água (100 mL) ou, se preferir, o comprimido poderá ser deglutido inteiro, sem a necessidade de dissolução prévia. A administração é por via oral. Granulado: 50 a 100mg (1/2 a 1 envelope dissolvido em um pouco de água ou suco) duas vezes ao dia, podendo alcançar até 200mg duas vezes ao dia. A administração é por via oral. Supositórios: 1 supositório de 100mg duas vezes ao dia, podendo alcançar até 200mg (2 supositórios de 100mg) duas vezes ao dia. Aplicar o supositório por via retal. Gotas: administrar 1 gota (2,5mg) por kg de peso, duas vezes ao dia, diretamente na boca da criança ou se preferir dilua em um pouco de água açucarada. Lembramos que cada gota contém 2,5mg de nimesulida e cada mL de NISULID contém 50mg de nimesulida. Cada mL do produto contém 20 gotas. Suspensão: a posologia recomendada é de 5mg/kg/dia - tradicionada a critério médico em duas administrações. Agitar antes de usar. Colocar a dose recomendada no copo-medida que acompanha o produto e pedir para a criança tomar pela boca (1mL da suspensão contém 10mg de nimesulida). Pacientes com insuficiência da função renal: não há necessidade de ajuste de dose em pacientes com insuficiência renal moderada. Em casos de insuficiência renal grave o medicamento é contra-indicado. Pacientes com insuficiência hepática: contra-indicado em pacientes com insuficiência hepática. VENDA SOB PRESCRIÇÃO MÉDICA. SE PERSISTIREM OS SINTOMAS, O MÉDICO DEVERÁ SER CONSULTADO. Material técnico científico de distribuição exclusiva à classe médica - Documentação Científica e informações adicionais estão à disposição da classe médica, mediante solicitação. MB_ 05 SAP4094207(A)09/09.

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acheflan

Cordia verbenacea DC. 5 mg/g

alfa-humuleno

CIÊNCIA E NATUREZA
CONTRA DORES MUSCULARES E INFLAMAÇÃO

Referências Bibliográficas: 1) Bula do produto ACHEFLAN: creme. Farmacêutico Responsável: Dr. Wilson R. Farias. Aché Laboratórios Farmacêuticos S.A. 2) BRANDÃO, D.C. et al. Estudo fase III, duplo-cego, aleatório, comparativo para avaliar eficácia e tolerabilidade da Cordia verbenacea e do diclofenaco dietilamônio, em pacientes portadores de contusões, entorses, traumas e lesões musculares, com início inferior a 24 horas. Revista Brasileira de Medicina, v.63, n.8, p.408-415, 2006. 3) REFSIO, C. et al. Avaliação clínica da eficácia e segurança do uso de extrato padronizado da Cordia verbenacea em pacientes portadores de tendinite e dor miofascial. RBM Revista Brasileira de Medicina, v.62, n.1/2, 40-46, 2005. 4) OLIVEIRA JÚNIOR, E.M. et al. Estudo piloto de avaliação da influência do ultrasom na estabilidade do alfa-humuleno e trans-cariofileno presentes no fitomedicamento antiinflamatório, creme de Cordia verbenacea 5 mg/g. Med Reabil, v.25, n.2, p.50-54, 2006. 5) Kairos Web Brasil. Disponível em: http://brasil.kairosweb.com.Acesso em: Dez/2016. 6) Invenções com Depósitos de Patentes junto ao INPI: Acheflan - PI8805094, PI0419105. 6) Disponível em:<http://www.redetec.org.br/inventabrasil/acheflan.htm>. Acesso em: Julho. 2014.

CONTRAINDICAÇÕES: INDIVÍDUOS SENSÍVEIS A CORDIA VERBENACEA DC. OU A QUALQUER COMPONENTE DA FÓRMULA. INTERAÇÕES MEDICAMENTOSAS: NÃO HOUVE RELATO DE INTERAÇÃO MEDICAMENTOSA NOS ESTUDOS CONDUZIDOS PARA AVALIAÇÃO DO ACHEFLAN.

ACHEFLAN. Cordia verbenacea DC - MS - 1.0573.0341. **Indicações: ACHEFLAN** é indicado nas seguintes situações: tendinites, afecções músculo-esqueléticas associadas à dor e inflamação, como dor miofascial (como dorsalgia e lombalgia), em quadros inflamatórios dolorosos associados a traumas de membros, entorses e contusões. **Contra-indicações: ACHEFLAN é contra-indicado nas seguintes situações: Indivíduos sensíveis a *Cordia verbenacea DC.* ou a qualquer componente da fórmula. Ocorrência de soluções de continuidade (feridas, queimaduras, lesões infeccionadas, etc). Advertências: ACHEFLAN** É PARA USO EXTERNO E NÃO DEVE SER INGERIDO. NÃO DEVE SER UTILIZADO ASSOCIADO A OUTROS PRODUTOS DE USO TÓPICO. RARAMENTE PODE CAUSAR AUMENTO DA SENSIBILIDADE LOCAL. TESTES REALIZADOS EM ANIMAIS INDICAM QUE **ACHEFLAN** NÃO APRESENTA ATIVIDADE IRRITANTE NA MUCOSA OCULAR. ENTRETANTO, RECOMENDA-SE LAVAR ABUNDANTEMENTE O LOCAL COM ÁGUA EM CASO DE CONTATO COM OS OLHOS. **Uso em idosos, crianças e outros grupos de risco:** não existe experiência clínica sobre o uso de **ACHEFLAN** em idosos, crianças abaixo de 12 anos, gestantes e lactantes. **Gravidez e lactação:** categoria de risco na gravidez C: Não foram realizados estudos em animais prenhes e nem em mulheres grávidas. "ESTE MEDICAMENTO NÃO DEVE SER UTILIZADO DURANTE A GESTAÇÃO OU AMAMENTAÇÃO SEM ORIENTAÇÃO MÉDICA". **Interações medicamentosas:** não houve relato de interação medicamentosa nos estudos conduzidos para avaliação do **ACHEFLAN**. Entretanto sua associação a outros fármacos deverá ser avaliada pelo médico. **Reações adversas:** O USO DE **ACHEFLAN** NÃO ESTÁ ASSOCIADO A RELATO DE REAÇÕES ADVERSAS. RARAMENTE PODE CAUSAR AUMENTO DA SENSIBILIDADE LOCAL. "ATENÇÃO: ESTE É UM MEDICAMENTO NOVO E, EMBORA AS PESQUISAS TENHAM INDICADO EFICÁCIA E SEGURANÇA ACEITÁVEIS PARA COMERCIALIZAÇÃO, EFEITOS INDESEJÁVEIS E NÃO CONHECIDOS PODEM OCORRER. NESTE CASO, INFORME SEU MÉDICO." **Posologia:** aplicação tópica, sobre a pele íntegra, de 8 em 8 horas. A duração do tratamento varia conforme a afecção que se pretende tratar. Nos ensaios clínicos a duração do tratamento variou entre 1 a 2 semanas podendo ser prolongado até 4 semanas. Farmacêutica Responsável: Gabriela Mallmann - CRF-SP nº 30.138. **VENDA SOB PRESCRIÇÃO MÉDICA.** MB03 SAP 4052805 e SAP 4053004

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TANDRILAX®

carisoprodol, cafeína
diclofenaco sódico, paracetamol

Uma relação de confiança se constrói com o tempo!

Referências Bibliográficas:1. Kairos Web Brasil. Disponível em: <http://brasil.kairosweb.com/index.html>.Acesso em: Dez/2016. **2.** Internal Report – CLOSE UP Dez/2016.

Contraindicação: Hipersensibilidade a qualquer dos componentes da fórmula. Interação Medicamentosa: A administração concomitante de glicocorticóides e outros agentes anti-inflamatórios não-esteróides pode levar ao agravamento de reações adversas gastrintestinais.

TANDRILAX é um medicamento. Durante seu uso, não dirija veículos ou opere máquinas, pois sua agilidade e atenção podem estar prejudicadas.

TANDRILAX (cafeína 30 mg / carisoprodol 125 mg / diclofenaco sódico 50 mg / paracetamol 300 mg) Comprimidos. USO ORAL. USO ADULTO. Indicações: Tratamento de reumatismo nas suas formas inflamatório-degenerativas agudas e crônicas; crises agudas de gota, estados inflamatórios agudos, pós-traumáticos e pós-cirúrgicos. Exacerbações agudas de artrite reumatóide e osteo-artrose e estados agudos de reumatismo nos tecidos extra-articulares e como coadjuvante em processos inflamatórios graves decorrentes de quadros infecciosos. **Contraindicações: Nos casos de úlcera péptica em atividade; hipersensibilidade a quaisquer dos componentes de sua fórmula; discrasias sanguíneas; diáteses hemorrágicas (trombocitopenia, distúrbios da coagulação), porfiria; insuficiência cardíaca, hepática ou renal grave; hipertensão grave. É contra-indicado em pacientes asmáticos nos quais são precipitados acessos de asma, urticária ou rinite aguda pelo ácido acetilsalicílico e demais inibidores da via da cicloxigenase da síntese de prostaglandinas. Precauções e Advertências: O uso em pacientes idosos, geralmente mais sensíveis aos medicamentos, deve ser cuidadosamente observado. Desaconselha-se o uso do TANDRILAX durante a gravidez e lactação. A possibilidade de reativação de úlceras pépticas requer anamnese cuidadosa quando houver história pregressa de dispepsia, hemorragia gastrintestinal ou úlcera péptica. Nas indicações do TANDRILAX por períodos superiores a dez dias, deverá ser realizado hemograma e provas de função hepática antes do início do tratamento e, periodicamente, a seguir. A diminuição da contagem de leucócitos e/ou plaquetas, ou do hematócrito requer a suspensão da medicação. Em pacientes portadores de doenças cardiovasculares, a possibilidade de ocorrer retenção de sódio e edema deverá ser considerada. Observando-se reações alérgicas pruriginosas ou eritematosas, febre, icterícia, cianose ou sangue nas fezes, a medicação deverá ser imediatamente suspensa. Não use outro produto que contenha paracetamol. Não é indicado para crianças abaixo de 14 anos, com exceção de casos de artrite juvenil crônica. Interações medicamentosas:** O diclofenaco sódico, constituinte do TANDRILAX, pode elevar a concentração plasmática de lítio ou digoxina, quando administrado concomitantemente com estas preparações. Alguns agentes antiinflamatórios não-esteróides são responsáveis pela inibição da ação de diuréticos da classe da furosemida e pela potenciação de diuréticos poupadores de potássio, sendo necessário o controle periódico dos níveis séricos de potássio. A administração concomitante de glicocorticóides e outros agentes antiinflamatórios não-esteróides pode levar ao agravamento de reações adversas gastrintestinais. A biodisponibilidade do TANDRILAX é alterada pelo ácido acetilsalicílico quando este composto é administrado conjuntamente. Recomenda-se a realização de exames laboratoriais periódicos quando anticoagulantes forem administrados juntamente com TANDRILAX, para aferir se o efeito anticoagulante desejado está sendo mantido. Pacientes em tratamento com metotrexato devem abster-se do uso do TANDRILAX nas 24 horas que antecedem ou que sucedem sua ingestão, uma vez que a concentração sérica pode elevar-se, aumentando a toxicidade deste quimioterápico. **Reações adversas: Distúrbios gastrintestinais como dispepsia, dor epigástrica, recorrência de úlcera péptica, náuseas, vômitos e diarréia. ocasionalmente, podem ocorrer cefaléia, sonolência, confusão mental, tonturas, distúrbios da visão, edema por retenção de eletrólitos, hepatite, pancreatite, nefrite intersticial. Foram relatadas raras reações anafilactóides urticariformes ou asmatiformes bem como síndrome de stevens-johnson e síndrome de lyell, além de leucopenia, trombocitopenia, pancitopenia, agranulocitose e anemia aplástica. o uso prolongado pode provocar necrose papilar renal. TANDRILAX é um medicamento. Durante seu uso, não dirija veículos ou opere máquinas, pois sua agilidade e atenção podem estar prejudicadas. Posologia:** A dose mínima diária recomendada é de um comprimido a cada 12 horas e a duração do tratamento deve ser a critério médico e não deverá ultrapassar 10 dias. Tratamentos mais prolongados requerem observações especiais (vide "Precauções"). Os comprimidos do TANDRILAX deverão ser ingeridos inteiros (sem mastigar), às refeições, com auxílio de líquido. "SE PERSISTIREM OS SINTOMAS O MÉDICO DEVERÁ SER CONSULTADO." VENDA SOB PRESCRIÇÃO MÉDICA - MS - 1.0573.0055 - MB 08 - SAP 4104203

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ALÍVIO COM[1,2]

dorene pregabalina

Rápido, eficaz e seguro no tratamento da fibromialgia.[3]

Redução da dor
a partir da primeira semana de tratamento na fibromialgia[4]

A pregabalina é eficaz
em reduzir a dor dos pacientes com fibromialgia[5]

Melhora da disfunção do sono
relacionada à fibromialgia.[6]
Grande parte desse benefício foi devido:[6]

- Efeito da pregabalina na insônia[6]
- Atividade analgésica do medicamento[6]

Referências Bibliográficas: 1) TOLLE, T. et al. Pregabalin for relief of neuropathic pain associated with diabetic neuropathy: a randomized, double-blind study. European Journal of Pain, v. 12, n. 2, p. 203-213, 2008. 2) OHTA, H. et al. A randomized, double-blind, multicenter, placebo-controlled phase III trial to evaluate the efficacy and safety of pregabalin in Japanese patients with fibromyalgia. Arthritis Research & Therapy, v. 14, N. 217, 2012. 3) BOOMERSHINE, C. S. Pregabalin for the management of fibromyalgia syndrome. Journal of Pain Research, v. 3, p. 81-88, 2010. 4) PAUER, L. et al. An international, randomized, double-blind, placebo-controlled, phase III trial of pregabalin monotherapy in treatment of patients with fibromyalgia. J Rheumatol, v. 38, n. 12, p. 2643-2652, 2011. 5) HEYMANN, R.E. et al. Consenso Brasileiro do tratamento da fibromialgia. Rev Bras Reumatol, v. 50, n.1, p.56-66, 2010. - A pregabalina é eficaz em reduzir a dor dos pacientes com fibromialgia (grau de recomendação A, nível de evidência 1b. Página 60, coluna 1, 5º parágrafo. - Consenso brasileiro do tratamento da fibromialgia, que inclui a pregabalina no tratamento da fibromialgia com grau de recomendação A e nível de evidência 1B. 6) RUSSELL, I.J. et al. The effects of pregabalin on sleep disturbance symptoms among individuals with fibromyalgia syndrome. Sleep Med., v. 10, n. 6, p. 604-610, 2009.

DORENE (pregabalina) 75 mg e 150 mg. Cápsula. USO ORAL. USO ADULTO E PEDIÁTRICO ACIMA DE 12 ANOS (vide Indicações). Indicações: Dor Neuropática; Epilepsia; Transtorno de Ansiedade Generalizada (TAG); Fibromialgia. Contraindicações: Dorene é contraindicado a pacientes com hipersensibilidade conhecida à pregabalina ou a qualquer componente da fórmula. Precauções e advertências: **Pacientes com problemas hereditários raros de intolerância a galactose, deficiência de lactase ou má- absorção de glicose-galactose não devem utilizar pregabalina cápsulas. Alguns pacientes diabéticos sob tratamento com pregabalina que obtiverem ganho de peso podem necessitar de ajuste da medicação hipoglicêmica. Houve relatos de reações de hipersensibilidade, incluindo casos de angioedema. Pregabalina deve ser descontinuado imediatamente se ocorrerem sintomas de angioedema, tais como edema facial, perioral ou da via aérea superior. O tratamento com pregabalina está associado com tontura e sonolência, que pode aumentar a ocorrência de acidentes (queda) na população idosa. Pacientes devem ser alertados para ter cautela até que os efeitos potenciais de pregabalina sejam familiares. Visão borrada transitória e outras alterações na acuidade visual foram reportadas por pacientes tratados com pregabalina. A descontinuação da pregabalina pode resultar na resolução ou melhora desses sintomas visuais. Foram observados sintomas de retirada em alguns pacientes após a descontinuação do tratamento prolongado e de curto prazo com pregabalina. Os seguintes eventos foram mencionados: insônia, dor de cabeça, náusea, ansiedade, hiperidrose e diarreia (vide item Reações Adversas). Como é o caso com qualquer droga ativa do SNC, deve-se avaliar cuidadosamente o histórico de pacientes quanto ao abuso de drogas e observá-los quanto a sinais de abuso da pregabalina. Foi relatada melhora da função renal após a descontinuação ou redução da dose de pregabalina. Houve relatos pós-comercialização de insuficiência cardíaca congestiva em alguns pacientes recebendo pregabalina. Devido aos dados limitados de pacientes com insuficiência cardíaca congestiva grave, Dorene deve ser administrado com cautela nesses pacientes (vide item 9. Reações Adversas).** Efeitos sobre a Habilidade de Dirigir e Operar Máquinas: Dorene pode produzir tontura e sonolência que, portanto, podem prejudicar a habilidade de dirigir e operar máquinas. Os pacientes devem ser aconselhados a não dirigir, operar máquinas complexas, ou se engajar em outras atividades potencialmente perigosas até que se saiba se este medicamento afeta a sua capacidade de executar tais atividades. Uso em Idosos, Crianças e Outros Grupos de Risco: Vide item Posologia. Gravidez e lactação: Uso durante a Gravidez: Não há dados adequados sobre o uso de pregabalina em mulheres grávidas. Estudos em animais mostraram toxicidade reprodutiva. O risco potencial a humanos é desconhecido. Portanto, Dorene não deve ser utilizado durante a gravidez. Métodos contraceptivos eficazes devem ser utilizados por mulheres com potencial de engravidar. **A pregabalina é um medicamento classificado na categoria C de risco de gravidez. Portanto, este medicamento não deve ser utilizado por mulheres grávidas sem orientação médica ou do cirurgião-dentista.** Uso durante a Lactação: Não se sabe se a pregabalina é excretada no leite materno de humanos. Entretanto, está presente no leite de ratas. Portanto, a amamentação não é recomendada durante o tratamento com Dorene. **Interações medicamentosas:** A pregabalina provavelmente não inibe o metabolismo de fármacos ***in vitro*** e nem se liga a proteínas plasmáticas. A pregabalina pode potencializar os efeitos do etanol e lorazepan. A pregabalina parece ser aditiva no prejuízo da função cognitiva e coordenação motora grosseira causado pela oxicodona. Em experiência pós-comercialização, houve relatos de insuficiência respiratória e coma em pacientes sob tratamento de pregabalina e outros medicamentos antidepressivos do SNC. Há relatos pós-comercialização de eventos relacionados à redução da função do trato gastrintestinal inferior (por ex, obstrução intestinal, íleo paralítico, constipação) quando a pregabalina foi coadministrada com medicamentos que têm o potencial para produzir constipação, tais como analgésicos opioides. Não foram conduzidos estudos de interação farmacodinâmica específica em voluntários idosos. Reações adversas: **As reações adversas mais comuns foram tontura e sonolência, em geral, de intensidade leve a moderada. As reações adversas comuns foram: Aumento de apetite, Confusão, desorientação, irritabilidade, humor eufórico, diminuição da libido, insônia, Ataxia, coordenação anormal, transtorno de equilíbrio, amnésia, distúrbios de atenção, dificuldade de memória, tremores, disartria, parestesia, sedação, letargia, Visão turva, diplopia, Vertigem, Vômitos, distensão abdominal, constipação, boca seca, flatulência, disfunção erétil, edema periférico, edema, marcha anormal, sensação de embriaguez, sensação anormal, fadiga e aumento de peso. As seguintes reações adversas foram relatadas durante a pós-comercialização: Sistema imune: angioedema, reação alérgica, hipersensibilidade. Sistema nervoso: dor de cabeça, perda de consciência, prejuízo mental.** Oftalmológicos: cerátite. Cardíacos: insuficiência cardíaca congestiva. Respiratório e torácico: edema pulmonar. Gastrintestinais: edema de língua, diarreia, náusea. Pele e tecido subcutâneo: inchaço da face, prurido. Renais e urinários: retenção urinária. Reprodutor e mamas: ginecomastia. Geral: mal-estar. Idosos (acima de 65 anos de idade). Num total de 998 pacientes idosos, não foram observadas diferenças quanto a segurança geral, em comparação aos pacientes com menos de 65 anos de idade. Posologia: Dorene deve ser utilizado por via oral, com ou sem alimentos. Cada cápsula de Dorene contêm 75 mg ou 150 mg de pregabalina. Dor Neuropática: A dose inicial recomendada de Dorene é de 75 mg duas vezes ao dia (150 mg/dia), com ou sem alimentos. Para a maioria dos pacientes, 150 mg duas vezes ao dia é a dose ideal. Com base na resposta individual e na tolerabilidade do paciente, a dose poderá ser aumentada para 150 mg duas vezes ao dia após um intervalo de 3 a 7 dias e, se necessário, até uma dose máxima de 300 mg duas vezes ao dia após mais uma semana. Epilepsia: A dose inicial recomendada de Dorene é de 75 mg duas vezes ao dia (150 mg/dia), com ou sem alimentos. Com base na resposta e tolerabilidade individuais do paciente, a dose poderá ser aumentada para 150 mg duas vezes ao dia após 1 semana. A dose máxima de 300 mg duas vezes ao dia pode ser atingida após mais 1 semana. Transtorno de Ansiedade Generalizada (TAG): A dose varia de 150 a 600 mg/dia, divididas em duas ou três doses. A necessidade para o tratamento deve ser reavaliada regularmente. Fibromialgia: A dose recomendada de Dorene é de 300 a 450 mg/dia. A dose deve ser iniciada com 75 mg duas vezes ao dia (150 mg/dia), com ou sem alimentos, e a dose pode ser aumentada para 150 mg duas vezes ao dia (300 mg/dia) em uma semana baseado na eficácia e tolerabilidade individuais. Descontinuação do Tratamento: Se Dorene for descontinuado, recomenda-se que isto seja feito gradualmente durante no mínimo 1 semana. Uso em Pacientes com Insuficiência Renal: A redução da dosagem em pacientes com a função renal comprometida deve ser individualizada de acordo com o clearance de creatinina. Para pacientes submetidos à hemodiálise, a dose diária de Dorene deve ser ajustada com base na função renal. Além da dose diária, uma dose suplementar deve ser administrada imediatamente após cada tratamento de 4 horas de hemodiálise. Uso em Pacientes com Insuficiência Hepática: Nenhum ajuste de dose é necessário para pacientes com insuficiência hepática. Uso em Crianças: A segurança e a eficácia de pregabalina em pacientes pediátricos abaixo de 12 anos de idade ainda não foram estabelecidas. O uso em crianças não é recomendado. Uso em Adolescentes (12 a 17 anos de idade): Pacientes adolescentes com epilepsia podem receber a dose como adultos. A segurança e a eficácia de pregabalina em pacientes abaixo de 18 anos de idade com dor neuropática não foram estabelecidas. Uso em Pacientes Idosos (acima de 65 anos de idade): Pacientes idosos podem necessitar de redução da dose de Dorene devido à diminuição da função renal. Dose Omitida: Caso o paciente esqueça de tomar Dorene no horário estabelecido, deve tomá-lo assim que lembrar. Entretanto, se já estiver perto do horário de tomar a próxima dose, deve desconsiderar a dose esquecida e tomar a próxima. **Este medicamento não pode ser partido, aberto ou mastigado.** SE PERSISTIREM OS SINTOMAS, O MÉDICO DEVERÁ SER CONSULTADO. **VENDA SOB PRESCRIÇÃO MÉDICA. SÓ PODE SER VENDIDO COM RETENÇÃO DA RECEITA.** MS - 1.0573.0457. MB 02_VP SAP 4475900.

Contraindicações: Dorene não deve ser utilizado se você tem hipersensibilidade (alergia) conhecida à pregabalina ou a qualquer componente da fórmula.
Interações medicamentosas: A pregabalina pode potencializar o efeito da oxicodona (analgésico), bebidas alcoólicas e de lorazepam (tranquilizante).

DORENE é um medicamento. Durante seu uso, não dirija veículos ou opere máquinas, pois sua agilidade e atenção podem estar prejudicadas.

CAC Central de Atendimento a Clientes
0800 701 6900
cac@ache.com.br
8:00 h às 17:00 h (seg. a sex.)

Campanha RESPEITO PELA PRESCRIÇÃO E PELA ADESÃO AO TRATAMENTO achê

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MATERIAL TÉCNICO CIENTÍFICO DE DISTRIBUIÇÃO EXCLUSIVA À CLASSE MÉDICA.
REVISTAS ACTAS DORENE CL.4 2017

achê
mais vida para você

Referências Bibliográficas: 1. Internal Report. Dados de auditoria IMS-PMB. Junho/2016. **2.** Bula do produto ARTROLIVE: cápsulas. Farmacêutica Responsável: Gabriela Mallmann. Guarulhos, SP. Aché Laboratórios Farmacêuticos S.A. **3.** Bula do produto ARTROLIVE: granulado em sachê. Farmacêutica Responsável: Gabriela Mallmann. Guarulhos, SP. Aché Laboratórios Farmacêuticos S.A. **4.** MARTEL-PELLETIER, J. et al. First line analysis of the effects of treatment on progression of structural changes in knee osteoarthritis over 24 months: data from the osteoarthritis initiative progression cohort. Ann Rheum Dis, v. 74, n. 3, p. 547-556, 2015.

Contraindicação: Pacientes que apresentem hipersensibilidade a quaisquer dos componentes de sua fórmula. Interação medicamentosa: É recomendável que pacientes diabéticos monitorem seus níveis sanguíneos de glicose mais frequentemente durante o tratamento com Artrolive.

ARTROLIVE CAPS. sulfato de glicosamina + sulfato de condroitina. MS – 1.0573.0286. **INDICAÇÕES:** ARTROLIVE é indicado para osteoartrite, osteoartrose ou artrose em todas as suas manifestações. **CONTRAINDICAÇÕES:** ARTROLIVE É CONTRAINDICADO EM PACIENTES QUE APRESENTEM HIPERSENSIBILIDADE A QUAISQUER DOS COMPONENTES DE SUA FÓRMULA, GRAVIDEZ E LACTAÇÃO. **PRECAUÇÕES E ADVERTÊNCIAS:** SÃO NECESSÁRIOS O DIAGNÓSTICO PRECISO E O ACOMPANHAMENTO CUIDADOSO DE PACIENTES COM SINTOMAS INDICATIVOS DE AFECÇÃO GASTRINTESTINAL, HISTÓRIA PREGRESSA DE ÚLCERA GÁSTRICA OU INTESTINAL, DIABETES MELLITUS OU A CONSTATAÇÃO DE DISTÚRBIOS DO SISTEMA HEMATOPOIÉTICO OU DA COAGULAÇÃO SANGUÍNEA ASSIM COMO PORTADORES DE INSUFICIÊNCIA DAS FUNÇÕES RENAL, HEPÁTICA OU CARDÍACA. SE OCORRER EVENTUALMENTE ULCERAÇÃO PÉPTICA OU SANGRAMENTO GASTRINTESTINAL EM PACIENTES SOB TRATAMENTO, A MEDICAÇÃO DEVERÁ SER SUSPENSA IMEDIATAMENTE. DEVIDO À INEXISTÊNCIA DE INFORMAÇÕES TOXICOLÓGICAS DURANTE O PERÍODO GESTACIONAL, ARTROLIVE NÃO ESTÁ INDICADO PARA SER UTILIZADO DURANTE A GRAVIDEZ. NÃO EXISTEM INFORMAÇÕES SOBRE A PASSAGEM DO MEDICAMENTO PARA O LEITE MATERNO SENDO DESACONSELHADO SEU USO NESSAS CONDIÇÕES E AS LACTANTES SOB TRATAMENTO NÃO DEVEM AMAMENTAR. PODE OCORRER FOTOSSENSIBILIZAÇÃO EM PACIENTES SUSCETÍVEIS, PORTANTO PACIENTES COM HISTÓRICO DE FOTOSSENSIBILIDADE A OUTROS MEDICAMENTOS DEVEM EVITAR SE EXPOR À LUZ SOLAR. FORAM DESCRITOS NA LITERATURA, ALGUNS CASOS DE HIPERTENSÃO SISTÓLICA REVERSÍVEL EM PACIENTES NÃO PREVIAMENTE HIPERTENSOS. NA VIGÊNCIA DO TRATAMENTO COM GLICOSAMINA E CONDROITINA, PORTANTO, A PRESSÃO ARTERIAL DEVE SER VERIFICADA PERIODICAMENTE DURANTE O TRATAMENTO COM ARTROLIVE. FORAM RELATADOS POUCOS CASOS DE PROTEINÚRIA LEVE E AUMENTO DA CREATINO-FOSFOQUINASE (CPK) DURANTE TRATAMENTO COM GLICOSAMINA E CONDROITINA, QUE VOLTARAM AOS NÍVEIS NORMAIS APÓS INTERRUPÇÃO DO TRATAMENTO. **INTERAÇÕES MEDICAMENTOSAS:** O tratamento concomitante com antiinflamatórios não-esteroides pode incorrer no agravamento de reações adversas do sistema gastrintestinal, sendo recomendado um acompanhamento médico mais rigoroso nesses casos. Alguns autores da literatura médica descrevem que o uso de glicosamina e condroitina pode incorrer em um aumento da resistência à insulina, porém, esses estudos foram realizados com doses muito superiores às indicadas na terapêutica clínica normal e sua validade ainda é discutida por vários outros autores. Estudos recentes demonstraram que a associação condroitina e glicosamina, quando empregada em pacientes portadores de diabetes mellitus tipo II, não levou a alterações no metabolismo da glicose. Os resultados destes estudos não podem ser extrapolados para pacientes com diabetes mellitus descompensado ou não-controlado. É recomendável que pacientes diabéticos monitorem seus níveis sanguíneos de glicose mais frequentemente durante o tratamento com ARTROLIVE. O uso concomitante de ARTROLIVE com os inibidores da topoisomerase II (etoposídeo, teniposídeo e doxorrubicina) deve ser evitado, uma vez que a glicosamina induziu resistência in vitro a estes medicamentos em células humanas cancerosas de cólon e de ovário. O tratamento concomitante de ARTROLIVE com anticoagulantes como o acenocoumarol, dicumarol, heparina e varfarina, pode levar ao aumento das chances de sangramento, devido a alterações nos valores de INR (International Normalized Ratio). Há relato de um caso na literatura de potencialização do efeito da varfarina, com consequente aumento dos valores sanguíneos de INR. Portanto, o uso concomitante de ARTROLIVE com anticoagulantes orais deve levar em conta avaliações rigorosas do INR. **Reações adversas: SISTEMA CARDIOVASCULAR:** EDEMA PERIFÉRICO E TAQUICARDIA JÁ FORAM RELATADOS COM O USO DA GLICOSAMINA, PORÉM NÃO FOI ESTABELECIDA UMA RELAÇÃO CAUSAL. FORAM DESCRITOS NA LITERATURA, ALGUNS CASOS DE HIPERTENSÃO SISTÓLICA REVERSÍVEL EM PACIENTES NÃO PREVIAMENTE HIPERTENSOS. NA VIGÊNCIA DO TRATAMENTO COM GLICOSAMINA E CONDROITINA, PORTANTO, A PRESSÃO ARTERIAL DEVE SER VERIFICADA PERIODICAMENTE DURANTE O TRATAMENTO COM ARTROLIVE. **SISTEMA NERVOSO CENTRAL:** MENOS DE 1% DOS PACIENTES EM ESTUDOS CLÍNICOS APRESENTARAM CEFALEIA, INSÔNIA E SONOLÊNCIA NA VIGÊNCIA DO TRATAMENTO COM A GLICOSAMINA. **ENDOCRINO-METABÓLICO:** ESTUDOS RECENTES DEMONSTRARAM QUE A ASSOCIAÇÃO CONDROITINA E GLICOSAMINA, QUANDO EMPREGADA EM PACIENTES PORTADORES DE *DIABETES MELLITUS* TIPO II, NÃO LEVOU A ALTERAÇÕES NO METABOLISMO DA GLICOSE. OS RESULTADOS DESTES ESTUDOS NÃO PODEM SER EXTRAPOLADOS PARA PACIENTES COM *DIABETES MELLITUS* DESCOMPENSADO OU NÃO-CONTROLADO. É RECOMENDÁVEL QUE PACIENTES DIABÉTICOS MONITOREM SEUS NÍVEIS SANGUÍNEOS DE GLICOSE MAIS FREQUENTEMENTE DURANTE O TRATAMENTO COM ARTROLIVE. **GASTRINTESTINAL:** NÁUSEA, DISPEPSIA, VÔMITO, DOR ABDOMINAL OU EPIGÁSTRICA, CONSTIPAÇÃO, DIARREIA, QUEIMAÇÃO E ANOREXIA TÊM SIDO RARAMENTE DESCRITOS NA LITERATURA NA VIGÊNCIA DE TRATAMENTO COM GLICOSAMINA E CONDROITINA. **PELE:** ERITEMA, PRURIDO, ERUPÇÕES CUTÂNEAS E OUTRAS MANIFESTAÇÕES ALÉRGICAS DE PELE FORAM REPORTADAS EM ENSAIOS CLÍNICOS COM GLICOSAMINA. PODE OCORRER FOTOSSENSIBILIZAÇÃO EM PACIENTES SUSCETÍVEIS, PORTANTO PACIENTES COM HISTÓRICO DE FOTOSSENSIBILIDADE A OUTROS MEDICAMENTOS DEVEM EVITAR SE EXPOR À LUZ SOLAR. **POSOLOGIA: Adultos:** Recomenda-se iniciar a terapêutica com a prescrição de 1 cápsula via oral 3 vezes ao dia. Como os efeitos do medicamento se iniciam em média após a terceira semana de tratamento deve-se ter em mente que a continuidade e a não-interrupção do tratamento são fundamentais para se alcançar os benefícios analgésicos e de mobilidade articular. **SE PERSISTIREM OS SINTOMAS, O MÉDICO DEVERÁ SER CONSULTADO. VENDA SOB PRESCRIÇÃO MÉDICA.** MB03a SAP447070. **ARTROLIVE** 1,5 g sulfato de glicosamina + 1,2 g sulfato de condroitina. MS – 1.0573.0286. **INDICAÇÕES: ARTROLIVE** é indicado para osteoartrite, osteoartrose ou artrose em todas as suas manifestações. **CONTRAINDICAÇÕES: ARTROLIVE** É CONTRAINDICADO EM PACIENTES QUE APRESENTEM HIPERSENSIBILIDADE A QUAISQUER DOS COMPONENTES DE SUA FÓRMULA, GRAVIDEZ E LACTAÇÃO. **PRECAUÇÕES E ADVERTÊNCIAS:** SÃO NECESSÁRIOS O DIAGNÓSTICO PRECISO E O ACOMPANHAMENTO CUIDADOSO DE PACIENTES COM SINTOMAS INDICATIVOS DE AFECÇÃO GASTRINTESTINAL, HISTÓRIA PREGRESSA DE ÚLCERA GÁSTRICA OU INTESTINAL, DIABETES MELLITUS OU A CONSTATAÇÃO DE DISTÚRBIOS DO SISTEMA HEMATOPOIÉTICO OU DA COAGULAÇÃO SANGUÍNEA ASSIM COMO PORTADORES DE INSUFICIÊNCIA DAS FUNÇÕES RENAL, HEPÁTICA OU CARDÍACA. SE OCORRER EVENTUALMENTE ULCERAÇÃO PÉPTICA OU SANGRAMENTO GASTRINTESTINAL EM PACIENTES SOB TRATAMENTO, A MEDICAÇÃO DEVERÁ SER SUSPENSA IMEDIATAMENTE. DEVIDO À INEXISTÊNCIA DE INFORMAÇÕES TOXICOLÓGICAS DURANTE O PERÍODO GESTACIONAL, **ARTROLIVE** NÃO ESTÁ INDICADO PARA SER UTILIZADO DURANTE A GRAVIDEZ. NÃO EXISTEM INFORMAÇÕES SOBRE A PASSAGEM DO MEDICAMENTO PARA O LEITE MATERNO SENDO DESACONSELHADO SEU USO NESSAS CONDIÇÕES E AS LACTANTES SOB TRATAMENTO NÃO DEVEM AMAMENTAR. PODE OCORRER FOTOSSENSIBILIZAÇÃO EM PACIENTES SUSCETÍVEIS, PORTANTO PACIENTES COM HISTÓRICO DE FOTOSSENSIBILIDADE A OUTROS MEDICAMENTOS DEVEM EVITAR SE EXPOR À LUZ SOLAR. FORAM DESCRITOS NA LITERATURA, ALGUNS CASOS DE HIPERTENSÃO SISTÓLICA REVERSÍVEL EM PACIENTES NÃO PREVIAMENTE HIPERTENSOS. NA VIGÊNCIA DO TRATAMENTO COM GLICOSAMINA E CONDROITINA, PORTANTO, A PRESSÃO ARTERIAL DEVE SER VERIFICADA PERIODICAMENTE DURANTE O TRATAMENTO COM **ARTROLIVE**. 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Os resultados destes estudos não podem ser extrapolados para pacientes com diabetes mellitus descompensado ou não-controlado. É recomendável que pacientes diabéticos monitorem seus níveis sanguíneos de glicose mais frequentemente durante o tratamento com **ARTROLIVE**. O uso concomitante de **ARTROLIVE** com os inibidores da topoisomerase II (etoposídeo, teniposídeo e doxorrubicina) deve ser evitado, uma vez que a glicosamina induziu resistência in vitro a estes medicamentos em células humanas cancerosas de cólon e de ovário. O tratamento concomitante de **ARTROLIVE** com anticoagulantes como o acenocoumarol, dicumarol, heparina e varfarina, pode levar ao aumento das chances de sangramento, devido a alterações nos valores de INR (International Normalized Ratio). Há relato de um caso na literatura de potencialização do efeito da varfarina, com consequente aumento dos valores sanguíneos de INR. 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Como os efeitos do medicamento se iniciam em média após a terceira semana de tratamento deve-se ter em mente que a continuidade e a não-interrupção do tratamento são fundamentais para se alcançar os benefícios analgésicos e de mobilidade articular. **SE PERSISTIREM OS SINTOMAS, O MÉDICO DEVERÁ SER CONSULTADO. VENDA SOB PRESCRIÇÃO MÉDICA.** MB03a SAP446702.

Material técnico-científico de distribuição exclusiva à classe médica.

A ação eficaz[1] no tratamento da Osteoartrite.

Glicolive
sulfato de glicosamina

Qualidade Aché e preço acessível para o tratamento da OA.[2-5]

Referências Bibliográficas: 1) MATHESON, A. J; PERRY, C. M. Glucosamine: a review of its use in the management of osteoarthritis. Drugs Aging, v. 20, n. 14, p. 1041-60, 2003. **2)** Kairos Web Brasil. Disponível em: http://brasil.kairosweb.com Acesso em: Agosto/16. **3)** Programa Cuidados pela Vida (" O Programa Cuidados pela Vida pode alterar ou interromper esta campanha sem aviso prévio". Desconto calculado sobre o Preço Máximo ao Consumidor)". **4)** Bula do produto GLICOLIVE: pó para solução oral. Farmacêutica Responsável: Gabriela Mallmann, Guarulhos, SP. Aché Laboratórios Farmacêuticos S.A. **5)** BRASIL. ANVISA. Agência Nacional de Vigilância Sanitária. Resolução - RE nº 1.101, de 9 de abril de 2015. Concede Certificação de Boas Práticas de Fabricação ao Aché. Diário Oficial da União, Brasília DF, p. 133, 9 abr 2015. **6)** Internal Report.

Contraindicações: hipersensibilidade a glicosamina ou a qualquer outro componente da fórmula. Interações medicamentosas: o sulfato de glicosamina pode favorecer a absorção gastrintestinal de tetraciclinas e reduzir a de penicilina e cloranfenicol.

GLICOLIVE é um medicamento. Durante seu uso, não dirija veículos ou opere máquinas, pois sua agilidade e atenção podem estar prejudicadas.

GLICOLIVE (sulfato de glicosamina) 1500 mg pó para solução oral. USO ORAL. USO ADULTO. **Indicações:** GLICOLIVE é indicado no tratamento deartrose ou osteoartrite primária e secundária e suas manifestações. Contraindicações: **GLICOLIVE é contra-indicado em pacientes com hipersensibilidade a glicosamina ou a qualquer outro componente da fórmula. Não deve ser utilizado durante a gravidez, lactação ou em fenilcetonúricos. Cuidados e advertências: informar ao médico caso esteja utilizando outros medicamentos. Recomenda-se cautela em pacientes com sintomas indicativos de distúrbios gastrintestinais, história de úlcera gástrica ou intestinal, diabetes mellitus, portadores de insuficiência renal, hepática ou cardíaca. Caso ocorra ulceração péptica ou sangramento gastrintestinal a medicação deverá ser suspensa imediatamente. Recomenda-se evitar a ingestão de bebidas alcoólicas, durante o tratamento.** Gravidez e lactação: não há dados com relação ao uso de GLICOLIVE na gravidez e lactação humana, portanto, seu uso não é recomendado nestes casos. Interações medicamentosas: o sulfato de glicosamina pode favorecer a absorção gastrintestinal de tetraciclinas e reduzir a de penicilina e cloranfenicol. Não existe limitação para administração simultânea de analgésicos ou anti-inflamatórios esteroides e não esteroides. **Reações adversas: os efeitos colaterais mais comuns são de origem gastrintestinal, de intensidade leve a moderada, consistindo em desconforto gástrico, diarreia, náusea, prurido e cefaléia. Reações hematológicas: não foram observadas alterações clínicas significativas.Testes laboratoriais: não se observaram diferenças significativas nos valores médios nem nos dados individuais das provas laboratoriais e constantes vitais. Glicolive é um medicamento. "Durante seu uso, não dirija veículos ou opere máquinas, pois sua agilidade e atenção podem estar prejudicadas."** Posologia: GLICOLIVE apresenta-se na forma de pó branco a levemente amarelado, com odor e sabor de abacaxi. Dispensar o conteúdo do envelope em um copo com água. Aguardar entre 2 a 5 minutos, mexer a solução com o auxílio de uma colher e consumir. Consumir 1 envelope por dia antes das refeições ou segundo indicação médica. A duração do tratamento fica a critério do médico. Para informações completas, consultar a bula na íntegra através da Central de Atendimento ao Cliente.VENDA SOB PRESCRIÇÃO MÉDICA. MS - 1.0573. 0403. MB05 SAP 4423401. "Material técnico científico de distribuição exclusiva à classe médica." SE PERSISTIREM OS SINTOMAS, O MÉDICO DEVERÁ SER CONSULTADO.

Artrosil
lisinato de cetoprofeno

SMR
SMART MODULATED RELEASE[3]

O ÚNICO lisinato de cetoprofeno[1]
com **TECNOLOGIA SMR[2,3]**

SEGURANÇA[2]
- Tolerabilidade gástrica 3 a 4 vezes maior comparado ao cetoprofeno comum.[2]

RÁPIDO INÍCIO DE AÇÃO[2]

EFICÁCIA[2]
- **Potência** anti-inflamatória, analgésica e antipirética superior ao cetoprofeno.[2]
- **Liberação prolongada:** Níveis plasmáticos mantidos por até 24h.[2,4]

Apresentações[4]
Cápsulas de liberação prolongada
de 160 e 320 mg com 10 e 20 cápsulas

Referências Bibliográficas: 1) ANVISA. Consulta de produtos. Disponível em: <http://www7.anvisa.gov.br/datavisa/Consulta_Produto/consulta_medicamento.asp>. Acesso em: Abr/2016. **2)** PELOGGIA, C.C.N.; BRITO NETO, A.J.; CUNHA, J. Avaliação da eficácia terapêuta e da tolerância do antiinflamatório lisinato de cetoprofeno, na forma cápsulas. Estudo multicêntrico aberto e não comparativo. Revista Brasileira de Medicina, v.57, n.6, p.617-624, 2000. **3)** Internal Report. **4)** Bula Do Produto ARTROSIL: Cápsulas. Farmacêutica Responsável: Gabriela Mallmann. Guarulhos, SP. Aché Laboratórios Farmacêuticos S.A.

Contraindicações: Úlcera péptica na fase ativa. Interações medicamentosas: Devido à elevada ligação de cetoprofeno com proteínas plasmáticas, é necessário reduzir a dosagem de anticoagulantes, fenitoínas ou sulfamidas quando administrados concomitantemente.

ARTROSIL (lisinato de cetoprofeno) - 160 mg e 320 mg - Cápsulas de liberação prolongada - Uso oral - Uso Adulto - Indicações: Artrose, coxartrose, espondiloartrose, artrite reumatóide, bursite, flebite e tromboflebite superficial, contusão, entorse, luxação, distensão muscular. **Contraindicações: Úlcera péptica na fase ativa, anamnese positiva de úlcera péptica recorrente, dispepsia crônica, gastrite, insuficiência renal grave, leucopenia e plaquetopenia, grave distúrbio de hemocoagulação.** Hipersensibilidade a quaisquer componentes de sua fórmula. Existe a possibilidade de hipersensibilidade cruzada com ácido acetilsalicílico ou outros fármacos anti-inflamatórios não-esteroidais. Portanto, o cetoprofeno não deve ser administrado a pacientes nos quais o ácido acetilsalicílico ou outros fármacos antiinflamatórios não-esteroidais tenham provocado sintomas de asma, rinite, urticária. O uso de lisinato de cetoprofeno é contra-indicado durante o primeiro e o último trimestre de gestação, pois pode causar hipertensão pulmonar e toxicidade renal no feto, característica comum aos inibidores da síntese de prostaglandinas. Pode também levar ao aumento do tempo de sangramento das gestantes e fetos e conseqüentemente eventuais manifestações hemorrágicas no recém-nascido. Há risco de retardar o trabalho de parto. **Precauções e advertências: O uso de cetoprofeno em pacientes com asma brônquica ou com diáteses alérgicas pode provocar uma crise asmática. Em pacientes com função renal comprometida, a administração de cetoprofeno deve ser efetuada com particular cautela levando-se em consideração a eliminação essencialmente renal do fármaco.** Embora não tenha sido observada experimentalmente toxicidade embriofetal com cetoprofeno nas doses previstas para uso clínico, a administração em mulheres grávidas, durante a amamentação ou na infância não é recomendada. **Interações medicamentosas: Devido à elevada ligação de cetoprofeno com proteínas plasmáticas, é necessário reduzir a dosagem de anticoagulantes, fenitoínas ou sulfamidas quando administrados concomitantemente.** O uso com ácido acetilsalicílico reduz o nível sérico de cetoprofeno e aumenta o risco de distúrbios gastrintestinais. No caso da administração com lítio há aumento de seu nível sérico podendo levar à intoxicação. Foi observado aumento da toxicidade do metotrexato em decorrência da diminuição de seu "clearance" renal. A probenecida reduz as perdas de cetoprofeno e aumenta seu nível sérico. A metoclopramida reduz a biodisponibilidade do cetoprofeno e pode ocorrer uma pequena redução de sua absorção no uso simultâneo com hidróxidos de magnésio ou alumínio. **Reações adversas: Assim como com outros antiinflamatórios não-esteroidais, podem ocorrer distúrbios transitórios, no trato gastrintestinal, tais como gastralgia, náusea, vômito, diarréia e flatulência**. Excepcionalmente foram observadas hemorragia gastrintestinal, discinésia transitória, astenia, cefaléia, sensação de vertigem e exantema cutâneo. O produto pode ser tomado às refeições ou com leite, a fim de evitar possíveis distúrbios gastrintestinais. **Posologia:** ARTROSIL 160 mg: Uma cápsula duas vezes ao dia durante ou após às refeições. A duração do tratamento deve ser a critério médico. ARTROSIL 320 mg: Uma cápsula ao dia durante ou após às refeições. A duração do tratamento deve ser a critério médico. SE PERSISTIREM OS SINTOMAS O MÉDICO DEVERÁ SER CONSULTADO. VENDA SOB PRESCRIÇÃO MÉDICA. MS – 1.0573.0128. MB_08 SAP 4057006.

Material técnico-científico de distribuição exclusiva a profissionais de saúde habilitados à prescrição e/ou dispensação de medicamentos.

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  Redução em torno de 30% a 40% na requisição de opioides
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- *17 MINUTOS [3]*
  Rápido início de ação*[3]
- **Maior tempo de ação*[3]**

PREÇO $ ACESSÍVEL

*** Trata-se de estudo realizado em modelo de dor de dente.**

Referências Bibliográficas: 1. ELIA, N.; LYSAKOWSKI, C.; TRAMER, M.R. Does multimodal analgesia with acetaminophen, nonsteroidal anti-inflammatory drugs, or selective cyclooxygenase-2 inhibitors and patient-controlled analgesia morphine offer advantages over morphine alone? Meta-analyses of randomized trials. Anesthesiology, v. 103, p. 1296-304, 2005. **2.** PERROT, S. et al. Efficacy and Tolerability of Paracetamol/Tramadol (325 mg/37.5 mg) Combination Treatment Compared with Tramadol (50 mg) Monotherapy in Patients with Subacute Low Back Pain: A Multicenter, Randomized, Double-Blind, Parallel-Group, 10-Day Treatment Study. Clinical Therapeutics, v. 28, n. 10, p. 1592-1606 , 2006. **3.** MEDVE, R.A.; WANG, J .; KARIM, R. Tramadol and acetaminophen tablets for dental pain. Anesth Prog. v.48, n.3, p.79-81 , 2001. **4.** Kairos Web Brasil. Disponível em: <http://brasil.kairosweb.com> Acesso em: Agosto/2016.

Contraindicações: hipersensibilidade ao tramadol, paracetamol ou a qualquer componente da fórmula ou aos opioides; intoxicações agudas pelo álcool, hipnóticos, analgésicos de ação central, opioides ou psicotrópicos; pacientes em tratamento com inibidores da monoaminoxidase (MAO) ou tratados com estes agentes nos últimos 14 dias. Interações medicamentosas: REVANGE® comprimido revestido não é recomendado como medicação pré-operatória obstétrica ou na analgesia pós-parto em lactantes, pois a segurança em lactentes e recém-nascidos não foi estudada.

REVANGE® é um medicamento. Durante seu uso, não dirija veículos ou opere máquinas, pois sua agilidade e atenção podem estar prejudicadas.

REVANGE®. cloridrato de tramadol e paracetamol. 37,5 MG + 325 MG comprimidos revestidos. USO ORAL. USO ADULTO. Indicações: dores moderadas a severas de caráter agudo, subagudo e crônico. **Contraindicações: hipersensibilidade ao tramadol, paracetamol ou a qualquer componente da fórmula ou aos opioides; intoxicações agudas pelo álcool, hipnóticos, analgésicos de ação central, opioides ou psicotrópicos; pacientes em tratamento com inibidores da monoaminoxidase (MAO) ou tratados com estes agentes nos últimos 14 dias. Cuidados e advertências: convulsões foram relatadas em pacientes recebendo tramadol na dose recomendada. Relatos espontâneos pós-comercialização indicam que o risco de convulsões está aumentado com doses de tramadol acima das recomendadas. A administração de tramadol pode aumentar o risco de convulsão em pacientes tomando inibidores da MAO, neurolépticos ou outros fármacos que reduzem o limiar convulsivo. REVANGE® comprimido revestido não deve ser administrado à pacientes dependentes de opioides. O tramadol reinicia a dependência física em alguns pacientes previamente dependentes de outros opioides. REVANGE® comprimido revestido deve ser usado com cautela e em dose reduzida em pacientes recebendo depressores do SNC como álcool, opioides, agentes anestésicos, fenotiazinas, tranquilizantes ou sedativos hipnóticos. REVANGE® comprimido revestido deve ser usado com bastante cautela em pacientes sob tratamento com inibidores da monoaminoxidase pois os estudos em animais mostraram aumento da incidência de óbito com a administração combinada de inibidores da MAO e tramadol. Precauções e advertências: REVANGE® comprimido revestido não deve ser administrado em conjunto com outros produtos à base de tramadol ou paracetamol. REVANGE® comprimido revestido deve ser administrado com cautela em pacientes sob risco de depressão respiratória. REVANGE® comprimido revestido deve ser usado com cautela em pacientes com pressão intracraniana aumentada ou traumatismo craniano. Alterações da pupila (miose) provocadas pelo tramadol podem mascarar a existência, extensão ou curso da patologia intracraniana. Gravidez e lactação: uso na gravidez e lactação: REVANGE® comprimido revestido somente deverá ser utilizado durante a gravidez se o potencial benefício justificar o potencial risco para o feto. Interações medicamentosas: REVANGE® comprimido revestido não é recomendado como medicação pré-operatória obstétrica ou na analgesia pós-parto em lactantes, pois a segurança em lactentes e recém-nascidos não foi estudada. Reações adversas: efeitos sobre a capacidade de dirigir e operar máquinas: mesmo quando usado de acordo com as instruções, REVANGE® comprimido revestido pode afetar a habilidade mental ou física necessária para a realização de tarefas potencialmente perigosas como dirigir ou operar máquinas, especialmente ao início do tratamento, na mudança de outro produto para REVANGE® comprimido revestido e na administração concomitante de outras drogas de ação central e, em particular, do álcool. REVANGE® é um medicamento. Durante seu uso, não dirija veículos ou opere máquinas, pois sua agilidade e atenção podem estar prejudicadas.** Os eventos adversos relatados com maior freqüência ocorreram no sistema nervoso central e gastrintestinal, sendo que os relatos mais comuns foram vertigem, náusea e sonolência. **Posologia:** a dose diária máxima de REVANGE® comprimido revestido é 1 a 2 comprimidos a cada 4 a 6 horas de acordo com a necessidade para alívio da dor, até o máximo de 8 comprimidos ao dia. A administração dos comprimidos pode ser feita independentemente das refeições. Nas condições dolorosas crônicas, o tratamento deve ser iniciado com 1 comprimido ao dia e aumentado em 1 comprimido a cada 3 dias, conforme a tolerância do paciente, até atingir a dose de 4 comprimidos ao dia. Depois disso, REVANGE® comprimido revestido pode ser administrado na dose de 1-2 comprimidos a cada 4-6 horas, até o máximo de 8 comprimidos ao dia. Nas condições dolorosas agudas, o tratamento pode ser iniciado com a dose terapêutica completa (1-2 comprimidos a cada 4-6 horas), até o máximo de 8 comprimidos ao dia. Pacientes com disfunção renal: em pacientes com "clearance" de creatinina inferior a 30 mL/min, recomenda-se aumentar o intervalo entre as administrações de REVANGE® comprimido revestido de forma a não exceder 2 comprimidos a cada 12 horas. VENDA SOB PRESCRIÇÃO MÉDICA. SÓ PODE SER VENDIDO COM RETENÇÃO DA RECEITA. Farmacêutica Responsável: Gabriela Mallmann CRF-SP 30.138. MS - 1.0573.0440. MB02 SAP 4389200.

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